THE JOURNAL
OF THE
American Medical Association

Subscription, $7.00 | PUBLISHED WEEKLY | Single Copies, 25 Cents

VOLUME 111, No. 24 | Copyright, 1938, by American Medical Association 535 North Dearborn Street, Chicago, Ill. | DECEMBER 10, 1938

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THE JOURNAL of the American Medical Association is published weekly by the American Medical Association, 535 North Dearborn Street, Chicago, Ill. Subscription price, $7.00 a year, 25c a copy. Canadian $8.50, Foreign $11.00. Entered as second class matter June 25, 1888, at the Postoffice at Chicago, Ill., under Act of March 3, 1879.

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The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 111, No. 24 — COPYRIGHT, 1938, BY AMERICAN MEDICAL ASSOCIATION CHICAGO, ILLINOIS — DECEMBER 10, 1938

THE RATIONAL TREATMENT OF ACUTE HEMATOGENOUS OSTEOMYELITIS

J. ALBERT KEY, M.D.

ST. LOUIS

The clinical picture and laboratory observations in acute hematogenous osteomyelitis are so well known to the average physician that a discussion of the diagnosis in this paper is not warranted. However, in a large percentage of the cases the diagnosis is not made until late in the disease. This is because the general practitioners and pediatricians who see the early cases are not osteomyelitis conscious. Consequently I would like to emphasize the facts that when a child suddenly becomes ill with fever and presents evidence of pain, disability and localized deep tenderness in an extremity osteomyelitis should be considered, and a negative x-ray examination does not rule out this disease.

This paper is presented because the disease is relatively frequent and not only carries a high mortality but usually causes prolonged illness in many of those who survive the acute attack and is an important factor in the production of crippling. While most surgeons have definite ideas as to the proper treatment of acute osteomyelitis, the treatment advised by authorities on the subject varies from that of the radical group, who recommend immediate emergency operation with adequate drainage of the focus in the bone, to that of the conservative group, who treat the patient for the general infection and more or less ignore the focus in the bone with the expectation that, as the patient's resistance is increased, the local disease will either heal spontaneously or form a subcutaneous abscess which can be drained by a small incision. There are, of course, all gradations between these two extremes, and a rather extensive study of recent literature leaves one very much confused. It is thought, then, that a rational consideration of the disease may tend to harmonize some of the wide differences of opinion.

The disease is caused by pyogenic bacteria which enter the blood stream from some focus (demonstrable in about 20 per cent of the patients) or are present as causal organisms in the blood stream and localize in the bone and begin to multiply. More than 90 per cent of the cases that occur are in children and it is generally believed that the usual site of the primary infection in the bone is in the metaphysis near the epiphysial line.

From the Department of Surgery of the Washington University School of Medicine.

Read before the Section on Orthopedic Surgery at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

In infants under 2 years of age the offending organism is a hemolytic streptococcus in about half of the cases and a staphylococcus in almost all of the remainder. In children over 2 years of age about 90 per cent of the cases are due to Staphylococcus aureus, and the streptococci account for most of the remainder. Either of these organisms may kill the patient promptly by an overwhelming general infection or more slowly over a period of weeks or may lead to prolonged suppuration with necrosis of bone, or an abscess may form which drains and heals or which heals without drainage.

It is thus obvious that there may be wide variations in the course and prognosis of individual patients, each of whom is suffering from an acute hematogenous osteomyelitis. These are due to that poorly understood condition which may be called the relation of the patient's resistance to the virulence of the organism. An increase in the patient's resistance or a decrease in the virulence of the organism will tend to cure the disease, and the converse also is true. Consequently, since "the first duty of the physician is to do no harm," care must be taken not to do anything to lower the patient's resistance even temporarily unless sufficient benefit will accrue to justify the procedure. It is accepted that an operation tends to lower the patient's resistance temporarily and that the ill effects vary directly with the amount of blood lost, the extent of the operation, the time consumed in performing it and the duration of the period of anesthesia.

The pyogenic cocci are characterized by their invasive qualities and by their ability to kill the tissues which they invade. This ability to spread into and kill the surrounding tissues is most evident when the focus is confined in the tissues and is relatively slight when the focus is on a surface or is adequately drained so that the growth of the organisms and the reaction of the tissues cannot generate pressure.

In the subcutaneous tissues infection with pyogenic cocci results in an acute inflammation. As the bacteria increase in number the adjacent cells are killed, autolysis occurs and pus is formed. The extravasation of fluid in the tissues, the dilatation of the blood vessels and the accumulation of phagocytic cells, especially leukocytes, and the proliferation of connective tissue cells cause swelling and tend to wall off and localize the infection. When the process occurs in a nonexpansile compartment, such as a bone, the changes mentioned are inhibited and the bacteria are enabled to invade and destroy the surrounding tissues with greater facility. It is also to be noted that in the subcutaneous tissues pain and tenderness occur early, while in the bone the focus is silent until the inflammation has reached the periosteum, because the interior of the bone is devoid of sensation, as can be demonstrated by infiltrating the

periosteum with procaine hydrochloride and drilling through the bone without causing pain.

It is thus apparent that by the time the infection causes pain and local tenderness the inflammation has spread through the cortex to the periosteum and that early drainage of the focus in the bone is desirable in order to inhibit the spread of the infection in the bone and the resultant extensive necrosis of bone. Early drainage of the focus in the bone is desirable not only because it tends to limit the local spread of the infection in the bone but also because it tends to cut off the supply of organisms at its source.

This brings up the question as to what is meant by the terms bacteremia and septicemia. I formerly considered bacteremia a condition in which bacteria were being fed into the blood stream from a focus and were being destroyed at about the same rate as that at which they entered the blood; the term septicemia I applied to a more severe condition in which the bacteria were actually multiplying in the blood stream. This distinction was purely theoretical and has been abandoned; and the two terms are used interchangeably to refer to a state in which bacteria enter the blood stream more rapidly than the defense mechanisms of the organism can destroy them, and it is probable that in certain instances the blood serves as a culture medium and the organisms actually multiply in the blood stream.

The source of the organisms in the blood stream is not an academic question but is of great practical importance because it determines the therapy in acute osteomyelitis. A large number of otherwise competent observers hold that since the bacteria reached the bone through the blood stream the patient is suffering primarily from a general infection and that the focus in the bone is merely incidental and should be ignored while the physician directs his therapy to the general infection. I have no patience with such reasoning. These patients were not sick until the focus developed in the bone, and they are now sick because they have a spreading infection in the bone which is feeding toxins and possibly bacteria into the circulation. If they have a demonstrable primary focus this merely served as a means by which a few bacteria got into the blood stream. It is not to be thought of as a funnel pouring a steady stream of bacteria into the blood. Had these few bacteria been taken care of in the usual way, nothing would have happened. But when some of them settled in the bone and started a spreading infection the disease began.

It is thus evident, I believe, that the local lesion should be drained. The next question is When should it be drained? It is argued that in the early stages the condition in the bone is analogous to a spreading cellulitis and that it is a fundamental principle of surgery not to incise a spreading cellulitis but to immobilize the part and apply local heat until the infection has localized and local tissue immunity has been established. By local immunity is meant a local concentration of opsonins which affect the bacteria in some manner and render them susceptible to the phagocytes. I do not believe that it has been established that there is sufficient local concentration of antibodies around a pyogenic infection to be of clinical importance. It is my impression that the localization of a pyogenic infection is an anatomic rather than an immunologic phenomenon and that it is due to the concentration of leukocytes and connective tissue cells and to the mechanical factors of vascular dilatation, edema and thrombosis. In a nonexpansile compartment, such as bone, there is considerable difficulty in the mechanical walling off of an infection, and the thrombi become septic and aid rather than hinder the spread of the disease.

While I do not recommend it, I do not believe that any particular harm is done by incising an area of cellulitis provided the tissues are not unduly traumatized and the part is treated properly afterward. In draining a deep abscess one incises through normal tissues and then a zone of cellulitis and is not concerned with the possibility of opening up blood or lymph channels that will permit the infection to reach the blood stream, nor is one concerned that the organisms from the deep abscess will invade and destroy the overlying normal tissues which have not established a local immunity. When the infection is in a tendon sheath or a joint it is drained immediately and one does not wait for these structures to be destroyed while the patient's resistance is increased to a point at which an equilibrium between it and the infection is established. Why should it be different in bone?

Furthermore, it is to be noted that infections in bone are not seen by surgeons as early as are severe infections in soft tissues, because the focus is silent until it spreads through the bone to the periosteum where it can affect sensory nerves and because the physicians who see them early are not osteomyelitis conscious and do not make the diagnosis early. In a series of 200 consecutive patients with chronic osteomyelitis who were admitted to the Shriners' Hospital for Crippled Children in St. Louis, Dr. McCarroll and I found that forty-one in whom an incorrect diagnosis had been made had been under treatment for from one to twelve weeks and that only nine had had the bone drained during the first week of the disease. It is thus evident that relatively few of these patients enter the hospital or are seen by a surgeon during the early stages of their illness, and the abscess in the bone is usually well established when they enter the hospital.

The question then arises as to whether they should be operated on immediately or treated conservatively. It is obvious that in a disease which varies so greatly in its severity and in its course the treatment cannot be standardized and that each patient must be considered as an individual problem which must be met according to the best principles of surgery.

CLASSIFICATION OF PATIENTS

From the standpoint of treatment, patients with acute hematogenous osteomyelitis may be divided into four overlapping groups: (1) patients with a mild infection who are not acutely ill, (2) severely ill patients with a spreading infection but in good general condition, (3) severely ill patients with a spreading infection and in poor general condition, and (4) patients in whom the infection has localized and is subsiding.

1. The treatment of patients who are not acutely ill need not be an emergency affair, but there is no reason why these patients should not be operated on and the bone drained as soon as convenient after the diagnosis is made. As a rule, these are patients in whom the infection is of relatively low grade, in whom there is very little danger that it will be widely disseminated in the bone and in whom the infection may form an abscess which can be drained subsequently or may even form an abscess in the bone which will heal spontaneously if they are left alone. On the other hand, if these patients are not treated a localized chronic osteomyelitis may develop which will demand radical treatment.

Consequently, I think it advisable to operate on such patients and drain the focus in the bone early in order to prevent the probable later chronic disease.

2. The severely ill patients with a spreading infection of the bone with high fever and marked toxemia are those seen relatively early in the disease but who are not dehydrated and whose general condition is good. A blood culture should be taken on admission, but one should not wait for the result, because it has no influence on the immediate treatment, which should be directed to the focus in the bone. In these cases I believe that waiting is not advisable because the pyogenic organisms are characterized by their tendency to invade and necrotize surrounding tissues, and if the patients are not operated on there will probably result a widespread destruction of bone with eventual development of a chronic osteomyelitis which may be difficult or impossible to heal. In addition to this there is the danger of involvement of the joint and the development of metastatic foci of infection. There is also the definite danger that leaving the abscess in the bone will tend to the production of a septicemia.

It is to be noted that I do not consider that a patient in whom hematogenous osteomyelitis develops has a primary septicemia but I feel that the septicemia which is so frequent in this disease is secondary to the infection in the bone. In other words, the constant presence of organisms in the blood stream means that these organisms are being fed into the blood stream more rapidly than the system of the patient is able to get rid of them and does not necessarily mean that one organism has got into the blood stream and has continued to multiply. The continued presence of the infection in the bone under pressure is one of the most favorable conditions for the development and continuance of such a septicemia, and even if a septicemia is present one of the most efficient methods of combating it is to cut off the supply of organisms to the blood stream by draining the focus in the bone. In such cases I recommend immediate operation with opening of the bone as gently as possible and with as little disturbance to the patient as possible. Under these conditions I have used local anesthesia and added epinephrine to the procaine hydrochloride and have found it possible to drain bony abscesses with but little harm to the patient.

After the operation the wound should be packed loosely with petrolatum gauze and the extremity should be immobilized in a large, hot, wet dressing and splint or in a plaster-of-paris cast, and fluids should be forced, if possible, or given intravenously or subcutaneously if necessary. Sufficient morphine or other sedative should be given to relieve the pain. To severely ill patients we have usually given repeated small transfusions and have not seen harm result from them, but I doubt whether they do any particular good in acute infections when there has been no significant loss of blood from the operation and when sufficient time has not elapsed for the production of a secondary anemia by the infection. Later, if a secondary anemia develops, transfusions are indicated to restore the blood volume or replace the cells that have been destroyed, but I am skeptical as to their value in supplying antibodies to combat the infection.

In infants under 2 years of age somewhat more leeway is allowed, and the operation may be delayed for four reasons: 1. The bone is more porous and the infection can more readily pass out through the bone and form extraosseous abscesses without sequestration. 2. Infants become dehydrated and toxic very quickly and most of them are badly in need of fluids when first seen. 3. Infants do not stand surgical operation as well as do older children and adults. 4. There is about an even chance that the infecting organism is a streptococcus which is susceptible to sulfanilamide.

3. Severely ill patients not in good general condition are usually patients who have had the disease for some time and are extremely toxic, are frequently delirious, are markedly dehydrated and have a high fever and a rapid, thready pulse. There is frequently a positive blood culture on admission. On this type of patient it is unwise to operate immediately, not because it is not desirable to drain the focus in the bone but because the patient's resistance is very low and has been taxed to the breaking point by the infection. Consequently it is better to put such a patient to bed, relieve his pain by morphine and immobilize the extremity, preferably with the application of a massive hot, wet pack and a splint with traction if it is practicable to do so. Fluids should be given immediately by mouth if possible or in the form of dextrose or salt solution intravenously if necessary.

If the patient is under 2 years of age there is about an even chance that the offending organism is a streptococcus and sulfanilamide in rather large doses may be started immediately without waiting for the blood or aspiration culture. This is because infants tolerate the drug well and because we delay operating on infants under conditions in which an older child would be operated on immediately. In children over 2 years of age we do not give the drug until we have obtained a positive culture of a streptococcus, because the chances are less than one in ten that it is a streptococcus and I believe that sulfanilamide may actually do harm in staphylococcic infections. Certainly I do not like the idea of operating on patients who are cyanotic from the drug, and these patients are going to be operated on because even in streptococcic infections I do not believe that it has been shown that sulfanilamide has much effect on a focus in a bone. In my limited experience it has not cleared up such foci, though it is possible that it may have helped to localize the disease.

In addition to the foregoing, one must consider immune serum, antitoxic serum, bacteriophage and toxoids. Bacteriophage has been recommended especially for staphylococcic septicemia. However, MacNeal's[1] figures give a mortality rate of 70 per cent, which is about the usual mortality of staphylococcic septicemia without bacteriophage, and since bacteriophage is inactive in blood serum I do not believe that it is worth while to try it.[2] Toxoids and vaccines are of no value in an acute infection and of questionable value in a chronic staphylococcic infection because, as is well known, the human organism shows little or no tendency to develop an immunity to the staphylococcus. The same is true of transfusions with blood from patients who have recovered from a similar disease or who have chronic osteomyelitis. These patients do not, in my experience, carry a high degree of immunity to the staphylococcus. In streptococcic infections it may be possible to find donors with sufficient opsonins to be of value, and if laboratory facilities and sufficient donors are available they should be checked for opsonins

1. MacNeal, W. J., and Frisbee, Frances C.: One Hundred Patients with Staphylococcic Septicemia Receiving Bacteriophage Service, Am. J. M. Sc. 191: 179-195 (Feb.) 1936.
2. Eaton, M. D., and Bayne-Jones, Stanhope: Bacteriophage Therapy, J. A. M. A. 103: 1769-1776 (Dec. 8), 1847-1853 (Dec. 15), 1934-1939 (Dec. 22) 1934.

against the offending organism and immunotransfusions should be given as suggested by Lyons.[3] Robertson[4] used an immune serum which he believes to be of some value. It should be given intramuscularly and not intravenously, since seven of Robertson's nine patients to whom it was given intravenously died. There is a staphylococcus antitoxin on the market and it is hoped that it will be of value in detoxifying these acutely ill patients; it may be used in large doses in order to get them into condition for operative drainage. Its use is still in the experimental stage.

The question next arises as to how long one should continue conservative treatment. This cannot be stated, but I believe that one should continue such treatment a matter of twelve hours or so until the patient appears to be getting better or worse. As soon as the patient has had some sleep and rest from the morphine and immobilization and as soon as his body fluids have been restored, I think that he should be operated on whether or not an abscess is present, provided a competent surgeon is at hand to perform the operation. The point is, I regard the deferring of the operation not as an attempt to permit the infection to localize but only as an effort to get the patient into better condition for the operation. Consequently, the waiting period is a matter of hours rather than of days.

4. In the last group of patients, in whom the infection has broken through the bone and formed an extraosseous abscess and whose acute illness is subsiding, I do not think it makes very much difference when they are operated on. However, the sooner the abscesses are drained the less likely are secondary foci to develop, although it is probable that by the time the acute condition has begun to subside there will be no further destruction of the bone. They really present a problem in chronic osteomyelitis and represent the group who have survived the so-called conservative treatment.

TYPE OF OPERATION

The type of operation varies with the condition found and with the age of the patient. In infants as little work as possible should be done on the bone. In children and adults it is important that adequate drainage of the focus within the bone be accomplished. It is stated that this can be done adequately by incising the periosteum. Starr[5] and his co-workers advocate drilling the metaphysis near and in the direction of the epiphysial line. If one is going to expose the bone I think that it does no harm to take out a window, especially as one is taking the window from the metaphysis where the cortex is quite thin, and if one uses sharp, thin osteotomes or large drills this can be done with relatively little trauma. The cavity is not curetted and no effort is made to remove the dead bone. The operation is for drainage only and is not a sequestrectomy. This gives a much better exposure of the underlying cancellous bone and is less apt to damage the epiphysial line. In confirmation of the likelihood of damaging the epiphysial line by drilling according to the method of Starr, Johnson's[6] report of seventy-three cases in which this method was used showed that there was disturbance of growth in 55 per cent.

In very ill patients the anesthetic should not be started until the surgeon is ready to make the incision, the operation should be as simple and brief as possible, and especial care should be taken not to traumatize the tissues unduly and a tourniquet is not applied.

After the operation the wound should be packed loosely with petrolatum gauze and the extremity immobilized either in a very large hot, wet dressing or in a plaster-of-paris cast, and the preoperative treatment just described should be continued.

In a diffuse infection in cancellous bone it is impossible to drain all of the area. Consequently, the temperature may be expected to fall gradually unless a septicemia is present. In certain cases the temperature will fall and then rise after a few days. This may be due to inadequate drainage of the primary focus, to extension of this focus or to the development of another focus. If another focus develops it should be drained as soon as it is recognized if the patient's condition warrants the operation. In cases in which drainage is established very early, and especially in those due to streptococci, the primary wound may heal without sequestration. In cases due to a staphylococcus in which there has been widespread destruction of bone there will be sequestration and chronic osteomyelitis which must be treated at a later date.

CONCLUSIONS

1. Early diagnosis is as important as it ever was in pyogenic infections of bone, and each case should be treated as an individual problem and according to the surgical principle that a deep abscess should be drained as early as possible provided the patient is in condition to stand the operation.

2. Not every case of acute osteomyelitis requires immediate operation, but every patient with this disease presents an acute surgical emergency and should be seen by a surgeon as soon as possible after the onset of the disease. The surgeon should decide when to drain the focus in the bone, and this decision may be a difficult one.

3. Early and adequate drainage of acute osteomyelitis is the most effective means of preventing chronic osteomyelitis.[7]

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ABSTRACT OF DISCUSSION

Dr. W. D. Gaessemer, Reading, Pa.: Dr. Key has given his treatment of this disease in a complete manner. Not all men will be in complete agreement with his views. Since most of these cases occur in children, diagnosis is often delayed until a period that precludes effective early treatment. The type and severity of the infection influence the treatment. In treatment, one may run the gamut from extreme conservatism to some form of radical procedure. The latter may vary from simple incision of the periosteum to drilling the medullary cavity or to extensive chiseling operations, with removal of the diseased cortex for drainage. Extreme conservatism is supported by a number of writers. A more radical course is advocated by others. However, nothing radical is done until local suppuration is very certain. Pyogenic osteomyelitis is not considered a surgical problem until this occurs. Fulminating cases, with few localizing signs, are fatal in spite of any treatment. In these one feels equally wrong in being radical or in just standing by. However, one should not in a routine manner delay primary operation, awaiting very marked local signs. Such surgical inactivity will increase an already appalling mortality.

3. Lyons, Champ: Immunotransfusion and Antitoxin Therapy in Hemolytic Streptococcus Infections, J. A. M. A. 108:1972-1975 (Dec. 14) 1935.

4. Robertson, D. F.: Acute Hematogenous Osteomyelitis, J. Bone & Joint Surg. 20:35-47 (Jan.) 1938.

5. Starr, C. L.: Acute Hematogenous Osteomyelitis, Arch. Surg. 44: 587-597 (May) 1932.

6. Johnson, R. A. Y.: Effect of Inflammation on the Epiphyses, Arch. Surg. 32:810 (May) 1936.

7. Key, J. A.: The Prevention of Chronic Osteomyelitis: Early Diagnosis and Treatment of Acute Osteomyelitis, J. Missouri State M. A. 35:39-43 (Feb.) 1938.

Neither should operation be extensive as a matter of routine. Its extent should be indicated by conditions found. Conservative, intelligent, exploratory operation with due consideration of all factors appears to be the best course and certainly can do no harm. Dr. Key's paper is a contribution to the treatment of these difficult cases.

DR. JESSE T. NICHOLSON, Philadelphia: Dr. Key has presented many of the perplexities encountered in the treatment of acute hematogenous osteomyelitis. He has given a classification of cases. He has found immediate operation necessary in but one group, the severely ill with a spreading infection but in good general condition. He has emphasized the role of the local bone focus as a source of toxin and bacteria which influence the general condition of the patient. These undoubtedly would be good reasons for immediate radical operation, but the results of conservative care and delayed operation make even these points controversial. In reviewing some of the recent papers on osteomyelitis one obtains the impression that early operation is hazardous to the patient. Green and Shannon found a mortality of 45 per cent following operation in infants under 6 months, and 21 per cent for all children under 2 years. They called attention to the high incidence of streptococcic infection at this age. This type of infection results in spontaneous formation of superficial abscesses and absence of sequestrum. By treating the general infection with blood transfusions, administration of increased fluids and simple incision of the abscess when it formed, the mortality was decreased to 3 per cent. Wilson and McKeever reviewed ninety cases including children over 2 years of age. In this group the staphylococcus was the common cause of the infection. When surgical drainage was done in the first seven days there was a 25 per cent mortality and after one week 9.7 mortality; in twenty-three cases in which spontaneous drainage occurred there was only one fatality. Even more conclusive was the recent report of Henry Brown of 160 cases before the Philadelphia Academy of Surgery. In the very toxic group, in which immediate operation was done, the mortality was 34 per cent. In very toxic cases in which surgery was delayed the mortality was 11 per cent. In the group of nontoxic cases there was no difference in mortality whether operation was immediate or delayed. The autopsies in cases in which death followed early operation proved by the evidence of multiple abscesses that the surgical procedure was futile. In the presence of blood stream infection there was a 51 per cent mortality. In cases in which a secondary blood stream infection developed following operation a 52 per cent mortality resulted.

DR. JOHN C. WILSON, Los Angeles: The situation resolves itself into treatment of infection irrespective of whether or not a bone abscess is present. Dr. Key said to me "You went so far in your paper as to advise the patients not to see a doctor." I do feel that when an abscess develops it should be drained, but all are familiar with cases of osteomyelitis that are opened in the first twenty-four or forty-eight hours in which no pus is encountered. The medullary canal contains a gray or serous exudate from which a positive culture of staphylococcus or streptococcus may be recovered. Those are the cases in which drainage should not be done. Whether or not septicemia is a primary or secondary factor is beside the point. An early drainage of these infections in the bone will, if the bacterial count in the blood culture is carefully observed, cause it to rise. I have seen this happen on a number of occasions. I have been following the bacterial count from day to day, and immediately after the drainage of the abscess the number of colonies per cubic centimeter of blood is markedly increased. It is my belief that the patients should be observed at least for a short time or until one finds out how the organism as a whole is reacting to this generalized infection. Blood cultures are of value to determine whether or not the patient is reacting properly. A gradual or rapid increase in the number of organisms recovered per cubic centimeter of blood indicates very closely that the patient's resistance is low. I cannot agree with Dr. Key that incision of a cellulitis or an infection which is not localized is without danger. Incision of a brawny, indurated area of skin and soft tissue is associated with great hazard. A little later on when this area softens and an abscess is formed it may be drained with impunity. The same situation occurs in bone. When the pus is present it should be evacuated, but all are aware that the evacuation of the abscess in the bone does not produce an immediate drop in temperature. It sometimes continues as long as six weeks after the drainage of the medullary canal before the temperature drops to normal. The plea that I wish to make is for the consideration of the patient as a whole and not of the individual bone lesion. The use of sulfanilamide has been mentioned. It probably has some place in the treatment of streptococcic infections but before using it one should know the type of organism that caused this particular difficulty. During the past year I have used immune rabbit serum in a few patients, apparently with some satisfactory results, but this must be continued for a further time before definite conclusions may be drawn.

DR. EARL D. MCBAIDE, Oklahoma City: I am seeing osteomyelitis in a much earlier stage and at a much younger age than I used to. It seems to me one ought to add just one more qualification to the type of common sense treatment. If the patient is a child in whom the abscess has already found its exit through the cortical bone but has not drained through the subfascial tissue or through the skin, it seems to me useless to expose the child to the dangers of an operation to open the bone further. One should simply drain the abscess of soft tissues under a local anesthetic and not try to do anything to the bone until a later date. After the child has regained strength, further drainage of the bone may be necessary. However, if it can be decided that the bone has not released the pressure by exit of its own accord, the bone should be drained surgically at that early stage in as cautious a manner as possible.

DR. WALTER G. STERN, Cleveland: I should like to ask Dr. Key whether he does not believe that in the stage of the disease which Dr. Wilson discussed—just before the abscess forms—if one just took a good, big, sharp, rotating burr and went into that area and out as quickly as one could, would one not, in an absolutely harmless manner, create a channel out of which the pus, when formed, may be readily drained, eliminating all tendency to back pressure and thus relieve the children of the danger of having those multiple foci that I so deplore?

DR. CHARLES F. NELSON, Beverly Hills, Calif.: The question of nutrition has been neglected in the discussion of the osteomyelitis situation. Why do these children have osteomyelitis? The reason is a developmental disturbance plus the lack of proper nutrition which is the vitamin and mineral balance. In my work on bone metabolism I have come to believe that a normal bone is never infected. Mineral imbalance probably precedes any bone disease. I have implanted staphylococci taken from cultures of osteomyelitis with septicemia into bone in animals, and the animals which have been kept on diets containing mineral and vitamin balance for a few weeks before the implantation suffered no ill effects while animals prepared on insufficient diets died. Osteomyelitis usually develops in children who are suffering from rickets or have some osteoporosis. The osteoid tissue present has almost no circulation. Without bone trabeculae there are no capillaries and this is the site where infection begins. Physicians should be reminded at once to establish vitamin and mineral balance, as marked general improvement of the child can be influenced immediately and local resistance about the foci of infection can be thrown out in a few days by the establishment of trabeculae with their accompanying capillaries. Most children with osteomyelitis have a latent tetany and their mineral balance should at once be established. I feel that the factor of developing resistance should be stressed. The question of drainage is an individual one. One should use every means of general sustenance until some definite evidence of localization has been established and then one should not be too destructive with surgical operation.

DR. J. ALBERT KEY, St. Louis: During the past year Dr. McCarrol and I reviewed 200 patients with chronic osteomyelitis who had been patients in the Shriners' Hospital, St. Louis. Of the 200 patients 50 per cent had joint involvement, 25 per cent had multiple foci, and 33⅓ per cent of the total number that we were able to treat over a period of three years were not cured at the end of three years. In other words, we cured only two thirds of those patients, and we could do anything that we wanted to with them. I may also add, for the benefit of the statistics, that we had no mortality among any of those patients, which I think is one answer to the mortality in statistics which

is seen elsewhere. Patients who enter with abscesses don't die. The patients of this group who were going to die died before they got to the hospital. The die is cast early in the disease in a certain number of persons who develop an acute pyogenic infection and there is nothing that anybody can do that will save them. There is also a group that are going to get well in spite of anything that we can do. There is a much larger group in whom we may influence the course of the disease. Early operation, if possible before pus is formed, will abort a considerable number of these cases of acute osteomyelitis, will prevent patients from getting extremely toxic and will save a lot of crippling in children. If the patient is too toxic to stand the operation, I think that one must wait until one can get the patient in as good condition as possible, not because one wants an abscess to form but because one wants to be able to operate on a patient who has a chance of surviving.

TREATMENT OF FRACTURE-DISLOCATION OF THE SPINE ASSOCIATED WITH CORD INJURY

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Injury to the cord by fracture-dislocation of the spine frequently demands that consideration be given to measures which will protect the cord from further injury by pressure of displaced bone. The impossibility of regeneration of the cord being accepted, it logically follows that the treatment of cord injuries, so far as restoration of function of the cord is concerned, is effective only in those cases in which the cord has not been entirely destroyed at the level of the vertebral lesion.

It is often stated that, because of the concussion and spinal shock associated with severe injuries to the cord produced by fracture-dislocation, it is impossible to make an early differentiation between complete physiologic interruption which may later show some recovery and a total transverse lesion which is permanent.[1]

It seems improbable that concussion is a factor of importance in cases of fracture-dislocation due to indirect violence. A better explanation of the instantaneous loss of function is contusion or crushing of the cord in the pia, which is rarely lacerated except in the most severe injuries. Laminectomy cannot improve the condition of the injured cord in such cases.

Compression of the cord is determined by the Queckenstedt test. The importance of this test in the study of injuries of the spinal cord was emphasized by one of us[2] in 1925. At this time we considered a positive subarachnoid block, demonstrated early by the Queckenstedt test, as an unequivocal indication for operation, unless the dislocation was so extensive as to show conclusively that the cord was crushed. Before the application of this test to the study of cord injuries there was little reliable data on which the indications for laminectomy might be based, and in many cases operation was done when there was no pressure on the cord. In the absence of compression on the cord, operation is not only futile but increases the damage to the spinal column already weakened by the injury. A larger experience with the Queckenstedt test has removed an earlier optimism with respect to the performance of laminectomy in those cases in which a fracture-dislocation has been suffered with immediate loss of all function of the cord below the site of the dislocation.

Examination of the cord at operation in complete lesions nearly always shows a sleeve of pia mater enclosing a softened, pulpy mass of disintegrated cord tissue, and pressure over the contused area after incision of the dura permits the finger to palpate the body of the vertebra with no resistance other than that offered by the pia alone.[3] In no case in our series has compression been due to extradural or extramedullary blood clot, although gross blood in the spinal fluid has been present in about one half of the cases. In a few cases due to direct force, the laminas are fractured and may be driven in on the cord. Fractures of the laminas with displacement and compression of the cord are more hopeful as a rule than fracture-dislocation. In severe incomplete cord lesions with compression from fractured laminas, prompt laminectomy may be of great benefit.

Partial or complete recoil of the displaced vertebrae toward normal alinement is the rule in fracture-dislocation of the spine. The greatest displacement continues only so long as the displacing force is in action, and the damage to the cord is generally completed when the dislocation reaches its maximum. On partial or complete recoil of the displaced vertebrae, bony pressure is reduced and may in some cases be completely removed from the injured cord. X-ray examination after recoil can give no information as to the extent of the displacement when the force was acting, so the gravity of the lesion must be determined by the patient's history and the evidence of impairment of function of the peripheral cord.

The history which the patient with a complete lesion usually gives is that with the impact of the injury he became paralyzed and lost all sensation in the lower extremities. If examination of the patient discloses absence of the Babinski reflex, deep sensibility, tactile sensation and deep reflexes distal to the lesion, our experience indicates that the injury to the cord is a hopeless one regardless of the treatment employed. The only recovery in such cases has been the return of some segmental innervation just below the level of the injury. For some years we have considered immediate and complete physiologic interruption of the cord from fracture-dislocation produced by indirect violence as an equivalent of anatomic transection.

Unconsciousness from an associated injury to the head or the mental confusion that sometimes results from lesions high on the cervical spine may render the patient incapable of giving an accurate history as to whether the injury produced complete and instantaneous loss of function of the cord below the lesion, and in some cases in which there is no unconscious state, mental confusion may make the tests for sensory and motor impairment

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Read before the Section on Orthopedic Surgery at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Spiller, W. G.: A Critical Summary of Recent Literature on Concussion of the Spinal Cord, with Some Original Observations, Am. J. M. Sc. 158, 1919.

2. Coleman, C. C.: Determination of Local Compression as an Indication for Laminectomy in Acute Injury of the Spinal Cord, J. A. M. A. 88:1106-1109 (Oct. 10) 1925; Further Observations on Spinal Block in Acute Cord Injury, Tr. South. S. A., 1925; contribution in Operative Surgery, Horsley, J. S., and Bigger, L. A., editors, Vol. 2, St. Louis, C. V. Mosby Company 2:1303-1311, 1937.

3. Thompson, J. E.: Pathological Changes Occurring in the Spinal Cord Following Fracture Dislocation of the Vertebrae, Ann. Surg. 78: 360 (Aug.) 1923.

unreliable. In such cases, provided there is pressure on the cord as demonstrated by the Queckenstedt test, it seems permissible to resort to operative measures to relieve the pressure, with the hope that the injury did not crush the cord and that the relief of pressure might result in some benefit to the patient. Cases of this type are unusual, but, in the absence of history indicating that the onset of paralysis was instantaneous, one may be justified in assuming that it was not immediately complete.

Spinal injuries are often overlooked in unconscious patients. The stiffness of a broken neck has frequently been attributed to the bloody spinal fluid from an intracranial injury until the persistent complaint of the patient after recovery from unconsciousness led to adequate x-ray studies. Injury of the cervical spine is so frequently associated with a combined injury of the head and shoulder that special attention should be given to the cervical spine when the unconscious patient has also sustained a fractured clavicle or injury to the shoulder girdle. We have seen a considerable number of cases in which there was a combination of head, cervical spine and shoulder injury.

Cord lesions from fracture-dislocation are rarely progressive. Experience shows that the maximum damage to the cord is usually manifested immediately, and, if the cord has not been crushed, considerable recovery extending over a long period may be expected. It is highly probable that the inherent tendency of the partial lesion to recover much of the function temporarily lost deserves the larger share of the credit for improvement following operation or manipulative procedures which decompress the spinal canal or restore vertebral alinement. It is difficult to evaluate the effect of operation in incomplete lesions, but certainly there is good reason to believe that the improvement in many cases due to the processes of repair has been erroneously attributed to laminectomy.

When we first applied the Queckenstedt test in 1923 for the determination of compression of the cord in cases in which there was complete paralysis, it was hoped that prompt relief of pressure would restore some function of the cord, and for a number of years laminectomy was done in all cases if the patient's condition permitted. The results have shown the operation to be futile in these cases for the reason that the damage is maximal at the time of impact and restoration of function is therefore impossible.

No satisfactory explanation can be offered here for the reported recovery after laminectomy of the occasional patient who is said to have immediately lost all cord function below the level of injury, but it may be suggested that an accurate history probably could not be obtained in these cases or that the neurologic examination was incomplete. It may also be that the criteria of a complete cord lesion as recognized by some writers might have been classified as incomplete by others. We have regarded an early positive Babinski reflex in the absence of any other signs of cord function distal to the lesion, as evidence that the lesion is not complete.

Herniation of the intervertebral disk into the spinal canal caused by fracture has been found in our series of injuries to the spinal cord. If the resulting cord lesion is instantly complete from the impact of the dislocated disk, it would seem that the prognosis would be practically the same as that of a complete lesion from fracture-dislocation in which the cord was crushed by displaced bone. The absence of x-ray evidence of deformity of the spinal column in severe injuries to the cord does not necessarily mean that a posterior dislocation of the cartilage has injured the cord. Vertebral recoil following extensive dislocation may have taken place, giving a practically normal roentgenogram, but the cord lesion may nevertheless be permanent.

USE OF SKELETAL TRACTION

Skeletal traction for the treatment of cervical fracture-dislocation suggested itself to one of us (C. C. C.) in June 1932 as a procedure of necessity in a case of telescoping fracture-dislocation of the axis on the third cervical vertebra without injury to the cord. Ordinary halter traction, so unsatisfactory as a method of cervical extension, could not be employed in this case because of an associated compound fracture of the skull and a compound comminuted fracture of the mandible. After weighing carefully the importance of reducing the exaggerated dislocation and the impossibility of applying traction by the methods then in use, we decided that the circumstances in the case required the application of extension tongs to the skull for the reduction of the dislocation. Edmonton tongs were applied to the skull in this case by our associate Dr. W. G. Crutchfield. It was obvious from the beginning that this type of traction was far more comfortable than that which we were accustomed to apply. X-ray examination showed widening of the intervertebral spaces and partial reduction of the dislocation by the skeletal traction. Functionally the results were excellent.

The principle of skeletal traction having been established, a most ingenious apparatus for the application of this type of traction in cervical injuries was devised by Dr. Crutchfield, and this apparatus carries out in a simple and more effective manner all the principles of the original conception. The technic of application and the results to be expected from skeletal traction by skull tongs have been discussed by Dr. Crutchfield [4] in a series of papers.

We have substituted skeletal traction for laminectomy in cases of complete cervical injuries with dislocation. We have seen no improvement in the function of the cord from the use of skeletal traction in these cases, and in this respect it has achieved no more than laminectomy. Skeletal traction, however, is a very minor procedure and carries practically no risk. It will reduce the dislocation and relieve the root pains, which may be very troublesome in some cases. It has therefore been used in complete lesions for the reduction of dislocation and relief of root pains and as a compromise between the futility of laminectomy and the policy of complete inaction, which is so unsatisfactory to the patient and his relatives.

INCOMPLETE LESIONS

The treatment of incomplete lesions of the cord offers a field for useful surgery provided there is pressure on the cord. Incomplete lesions of the cervical region with fracture-dislocation may be treated by skeletal traction for from eighteen to twenty-four hours. After this time, if the cord lesion is stationary or increasing and the block continues, laminectomy is indicated. In cases of cervical dislocation with mild

4. Crutchfield, W. G.: Skeletal Traction for Dislocation of the Cervical Spine, South. Surgeon 1: 154-159 (June) 1933; Fracture-Dislocations of the Cervical Spine, Am. J. Surg. 30: 392-398 (Dec.) 1935.

or no injury to the cord, reduction of the dislocation by skeletal traction is the ideal treatment. Recurrence of the dislocation may be prevented by appropriate orthopedic measures.

A subarachnoid block caused by cervical fracture-dislocation, in our experience, is not usually removed even though the dislocation is completely reduced by skeletal traction. With regard to incomplete cord injuries of the dorsal or upper lumbar region, we are not prepared to express an opinion as to the effect of hyperextension on a subarachnoid block, since we prefer laminectomy as a primary procedure in such cases. It should be said, however, that a review of the literature indicates that hyperextension in the treatment of compression fractures of the dorsal and lumbar regions with associated injury of the cord or cauda equina is often satisfactory. It appears that hyperextension in some hands has superseded laminectomy in the treatment of these cases.

Restoration of the alinement of the vertebral column at any level may leave a contused swollen cord compressed and incarcerated by the dura. The continuing block after reduction of the dislocation may be demonstrated by the Queckenstedt test. In such a situation there would not be complete relief of circulatory impairment in the contused cord segments, and as a result an incomplete lesion might become progressive. If symptoms of impairment of the cord are not ameliorated by reduction of the dislocation, or if the symptoms should increase and the block continue, indications for laminectomy are as urgent as if there had been no reduction of the dislocation.

The fear of producing further injury to the cord by manual reduction of a cervical dislocation in partial injuries is well founded, and it is difficult also to free one's mind of considerable apprehension for the fate of the cord when compression fracture-dislocations of the dorsal and upper lumbar regions with incomplete cord injury are reduced by hyperextension. If the dorsal canal has been narrowed by the injury and particularly if there is a fracture of the laminas or pedicles, further encroachment on the canal, however slight, from manipulation of the vertebral segments, might result in an increase of paralysis or even a total loss of cord function. The withholding of an anesthetic during the manipulation incident to manual reduction of cervical dislocations or hyperextension of the dorsal and lumbar lesions is of little protection against further injury to the cord. Should pressure on the cord be suddenly increased by the manipulation, the damage is instantaneous, just as in the case of complete lesions from fracture dislocation in which the crushing of the cord is coincident with the impact of the dislocating vertebra. The gradual unlocking of a cervical dislocation by skeletal traction is not attended by the risk of further injury to the cord. In this respect it is in marked contrast to manual reduction of cervical dislocations and hyperextension procedures for the relief of dorsolumbar lesions.

It is of some importance to determine the proper sequence of the steps in the treatment of incomplete dorsal injuries, associated with compression fractures. It would be most helpful to know whether a severe incomplete lesion with pressure on the cord can be more safely managed first by hyperextension and then by laminectomy if the compression is not relieved, or whether the order of these procedures should be reversed. Because of the limitation of x-ray studies in disclosing the position of the fragments of bone and their possible encroachment on the dura, it must be assumed that evidence of complete block associated with fracture-dislocation is an indication that further encroachment on the cord may result in increased damage to this important structure. For this reason it would seem safer in these cases to perform a laminectomy to give greater protection to the cord before hyperextension is attempted. There should be little hesitation in using hyperextension for reduction of deformity in immediately complete lesions of the dorsal cord. The correction of deformities due to compression fracture and dislocation, particularly in the lower dorsal and lumbar regions, is highly desirable even with irreparable cord lesions because of the longer duration of life and the wider range of activities which these patients may have, as contrasted with complete lesions of the upper dorsal and cervical regions. It is true that the reduction of a dislocation above the cauda equina cannot be expected to bring about improvement in those cases in which the lesion shows immediate and complete loss of cord function, but hyperextension may restore the column to normal alinement and prevent root pains.

Laminectomy for injuries involving the cauda equina is not restricted by the limitations which experience has imposed in the treatment of lesions of the cervical and dorsal cord. The cord, being a solid cylindric structure, is more vulnerable to a compressing force than the bundle of roots which comprise the cauda equina. Moreover, the cauda equina has a greater capacity for resisting the effects of injury, and the motor roots possess the power of regeneration under favorable conditions even after severe injury or complete division. The relief of compression, while not benefiting the sensory roots already destroyed, may protect others not so badly damaged from progressive injury due to pressure of a deformed column. Laminectomy is therefore indicated in fracture-dislocation of the lumbar spine involving the cauda equina, even when a complete nervous lesion appears to have been immediately produced. Delay in operating on lesions of the cauda equina is likely to add to the damaging compression complications due to formation of adhesions, making an adequate operation extremely difficult or even impossible.

The technic of laminectomy for injuries to the cord may be briefly considered. The greatest care is necessary in handling the patient and transferring him to the operating table to avoid further injury to the cord. Local anesthesia is generally satisfactory and is preferred, especially in cervical operations. In injuries high on the cervical spine the use of morphine should be avoided. Before the operation the fluid below the compression is removed by lumbar puncture and replaced by air. The disclosure of the subarachnoid air after the dura is opened promptly indicates that the lower level of the compression has been relieved, while the free escape of fluid from above shows that the highest level of the compression has been removed. In fracture of the laminas the greatest care is necessary in separating the attachment of the muscles and in removing the bone to avoid further damage to the cord. Wide separation of the muscles from each side is generally unnecessary and should be avoided whenever possible. Hemorrhage from the muscles is controlled

entirely by the electrocautery, and in no operation is this equipment more useful. The level of the greatest bone compression is usually determined by x-ray study before operation and verified by the appearance of the column after operative exposure. The laminas adjacent to those of the displaced vertebrae are first removed and the arch compressing the cord is reserved for removal last, as an added protection to the underlying cord. Incision of the dura should begin above or below the level of compression and continue until the constriction of the cord is entirely relieved. In some cases of pressure by fragments of laminas it is unnecessary to open the dura. If opened, however, and this is usually required in contusion of the cord, no effort is made to suture the dura. In some cases traction combined with simultaneous pressure over the displaced vertebra in the proper direction may restore alinement during the laminectomy. Drainage is rarely required.

After cervical laminectomy, the head, neck and upper part of the chest should be immobilized by a plaster shell extending from the occiput to the lower lumbar region. The advisability of fixation in hyperextension after laminectomy for dorsal and lumbar injuries should be determined in consultation with the orthopedist.

MANAGEMENT OF SEVERE INJURIES

The general management of patients with severe cord injuries is obviously of the greatest importance. Pressure sores may be prevented by careful nursing and the use of cork or air mattresses. The complication of bedsores and infection seriously retards the progress of an incomplete lesion, delays or prevents the advent of an automatic bladder in the complete lesions and adds enormously to the problems of nursing care and expense of treatment. In our series of cases various methods of management of the paralyzed bladder have been tried. Intermittent catheterization, the use of a retention catheter, allowing the bladder to overflow, and suprapubic cystostomy have all been given a fair trial. The value and disadvantages of all these methods have been carefully considered, and we have adopted suprapubic cystostomy with drainage as a routine measure for all male patients with paralysis of the bladder due to an injury to the cord. This method has seemed to give the patient a greater protection from infection of the bladder and kidneys, and at the same time it has simplified the general nursing care of the patient. A retention catheter is nearly always followed by some form of genito-urinary infection in the male, but it is entirely satisfactory in the paralyzed female patient.

In our clinics all patients with a spinal injury are admitted primarily to the neurosurgical service. If the patient has a cord injury, a careful neurologic examination together with adequate x-ray study and the Queckenstedt test is promptly made to determine whether laminectomy is required. It may be necessary to repeat the Queckenstedt test several times before a decision can be made as to whether operation is indicated. Cases showing no involvement of the cord are transferred to the orthopedic service. All hyperextension procedures for injuries with or without associated impairment of the cord are conducted by the orthopedic department. Our urologic and orthopedic colleagues have generously cooperated in the management of these cases.

In a series of 259 consecutive patients admitted to one of our clinics (Medical College of Virginia) in a five year period ended Jan. 1, 1938, during which time skeletal traction for cervical dislocation was originated, there was a group of eighty patients with cord lesions or root injuries involving important peripheral nerves. The location of these lesions was as follows: fifty-three cervical, fourteen thoracic and thirteen lumbar. There were thirty-one patients with complete cord lesions, twenty-four of whom died in the hospital. There was no improvement in the function of the cord in any of these cases. There were forty-nine incomplete cord lesions with twelve hospital deaths. Associated injuries rather than the cord lesion were responsible for death in a number of the latter cases. The incidence of associated injuries was high (twenty-four cases).

Laminectomy was performed in ten of the eighty cases analyzed in this paper. There were five laminectomies in the cervical region and five below this level. Of the cervical laminectomies, four were fatal or unimproved. The case in which there was improvement was incomplete and presented a subarachnoid block as the indication for laminectomy. Of the five patients who had laminectomies performed for dorsal or lumbar injuries or both, three were improved, one was unimproved and one died of urinary sepsis. Skeletal traction was employed in twenty-four cases of the group presenting cervical dislocation associated with injury to the cord or severe root involvement, and sixteen of these patients died or were unimproved while eight patients showed improvement. In the series, twenty-one patients were treated by orthopedic measures alone.

Statistics on injuries to the cord associated with fracture-dislocation are of little value as a guide to treatment, but a study of the group of eighty cases analyzed in the preparation of this paper corroborates fully an impression we have held for some years, while dealing with a much larger number of cord injuries, that surgery has a limited application in the treatment of such lesions.

SUMMARY

1. Laminectomy for injury to the spinal cord due to fracture-dislocation is indicated only for the relief of localized compression of the cord which has not been destroyed at the level of the injury.

2. Compression of the cord can be determined accurately only by the Queckenstedt test. If the test is negative there is no indication for operation in closed injuries, regardless of the severity of the lesion. If the test is positive, laminectomy is indicated only if one believes that the cord possesses some capacity for recovery.

3. Lesions of the cord producing immediate and complete physiologic interruption have, in our experience, shown no indication of recovery regardless of the treatment employed. We have come to regard operation in these cases as a futile procedure.

4. Reduction of the dislocation in the cervical region by skeletal traction, while not improving the patient's chances for restoration of cord function in complete cord lesions, is in such cases useful for the relief of root pains. It is a practical and simple substitute for laminectomy.

5. Severe incomplete cervical cord lesions showing compression with stationary or increasing symptoms may be treated for from eighteen to twenty-four hours by traction. If the symptoms are unchanged and pressure persists after this time, laminectomy under local anesthesia is indicated while traction is being maintained.

6. Severe incomplete lesions of the dorsal region with a block require laminectomy. If there is a compression fracture or fracture-dislocation with a block, laminectomy should precede hyperextension.

7. Prompt laminectomy is indicated in complete lesions of the cauda equina with compression caused by fracture-dislocation.

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ABSTRACT OF DISCUSSION

DR. FREDERIC C. BOST, San Francisco: It is indeed a privilege to hear from any one who has had as many as 250 cases of spinal injury in a five year period. I think you will all agree with me that such an experience ought to be worth a great deal to all of us. I know of no more serious injury that confronts me as an orthopedist than cervical spine injuries. As soon as one sees a patient with a fracture dislocation of the cervical spine or other portion of the spine, particularly with complete cord injury, one is confronted with a lot of questions. Dr. Coleman and Dr. Meredith in their paper have answered all these questions. It is brought out clearly that the Queckenstedt test, a careful history of the period immediately following injury and a thorough neurologic examination will allow it to be determined whether or not laminectomy is indicated. In the other cases one may resort to skeletal traction. Skeletal traction may be used with the Crutchfield tongs or by any other method which one may desire. One may hope to reduce the fracture-dislocations of the cervical spine without running the danger of doing further damage to the already injured cord. The authors have also brought out clearly the pathologic changes that follow cord injury, and when one realizes what these are one will know that laminectomy can offer but little in a complete cord lesion. We, therefore, as surgeons may follow a policy of nonsurgical intervention rather than subjecting the patient to something that may do him no good. A careful perusal of this paper will show that the principles which it enunciates will allow us to establish a nice regimen on which these patients can be handled.

DR. C. C. COLEMAN, Richmond, Va.: I thank Dr. Bost for his discussion. I should like to correct the erroneous impression he received from my paper as to the number of cases. It is true that we have had 259 cases of spinal injuries in one group of hospitals (Medical College of Virginia) in a five year period, but not 250 cervical injuries as he evidently understood us to say. I am quite sure that he will find the statement in the original paper as to the number of cord injuries as well as the number of spinal injuries in which the cord was not involved.

The Insulin Molecule.—Another hormone which evidently has its origin in the amino acids of the blood is insulin. In contrast to thyreoglobulin, which yields thyroxine, insulin appears to contain no prosthetic group to which its physiological action may be attributed. Intensive investigations designed to disclose the presence of some peculiar constituent of unusual potency have merely served to emphasize the typical protein nature of the substance. From hydrolysates of the crystalline compound nine amino acids have been separated and identified. These are cystine, tyrosine, glutamic acid, leucine, arginine, histidine, lysine, phenylalanine and proline. Although the above are among the most commonplace components of originary proteins, they are said to account for practically the entire insulin molecule. The unique properties of the hormone evidently are due to the structural arrangement of its constituents. In this connection it is of interest to note that many enzymes, particularly those which effect hydrolytic changes, appear to be simple proteins and that their activity is to be ascribed to peculiarities in the disposal of the amino acids within the molecules rather than to the presence of prosthetic groups. According to Northrop, "the formation of enzymes is a special case of the more general problem of the synthesis of proteins."—Rose, William C.: The Physiology of Amino Acid Metabolism, *Proc. Inst. Med. Chicago* **12**:98 (April 15) 1938.

SULFANILAMIDE IN THE TREATMENT OF 106 PATIENTS WITH MENINGOCOCCIC INFECTIONS

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The observation of Buttle and his associates [1] that sulfanilamide protected and cured mice of an experimentally induced meningococcic septicemia has been amply confirmed by Proom,[2] Rosenthal and his associates,[3] Levaditi and Vaisman [4] and Brown.[5] Branham and Rosenthal [3] and Brown [5] concluded as a result of their observations on experimental meningococcic infections in mice that a combination of sulfanilamide with an effective antimeningococcus serum produced a greater protective or therapeutic effect than either of the agents by itself. Schwentker, Gelman and Long [6] in a preliminary report considered sulfanilamide to be as effective in the treatment of meningococcic infections in human beings as good specific antiserums. All of their eleven patients with but one exception were treated by both the parenteral and the intrathecal route. In this group of eleven patients there was but one death.

Since this report was published, McIntosh and his co-workers,[7] Mitchell and Trachsler,[8] Bernstein,[9] Carey,[10] Basman and Perley [11] and Brennemann [12] have reported that patients ill with meningococcic infections and treated with sulfanilamide have made definite recoveries from their disease. Pongratz [13] has reported recoveries in three patients suffering from meningococcic meningitis who were treated with prontosil [14] parenterally and perorally and with serum by the intrathecal route.

Willien [15] treated five patients ill with meningococcic infection with sulfanilamide. He states that "the clinical response of the patients to treatment with sulfanilamide was satisfactory in every case" and that a favorable outcome was achieved "even with oral administration alone."

Recently Eldahl [16] has reported on the therapeutic use of sulfanilamide in twelve patients suffering from severe forms of meningococcic meningitis. Nine of these patients recovered. All twelve patients were treated by the intramuscular and intrathecal routes. In this paper Eldahl reaches the conclusion that sulfanilamide "has but little effect if the remedy is administered exclusively by mouth or intramuscularly." This statement is in contradiction to the observations of

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From Sydenham Hospital, Baltimore City Health Department.

1. Buttle, G. A. H.; Gray, W. H., and Stephenson, D.: Lancet **1**:1286 (June 6) 1936.
2. Proom, H.: Lancet **1**:16 (Jan. 2) 1937.
3. Rosenthal, S. M.; Bauer, J., and Branham, S. E.: Pub. Health Rep. **52**:662 (May 21) 1937. Branham, S. E., and Rosenthal, S. M.: ibid. **52**:685 (May 28) 1937.
4. Levaditi, Constantin, and Vaisman, A.: Compt. rend. Soc. de biol. **125**:604, 1937.
5. Brown, T. M.: Bull. Johns Hopkins Hosp. **61**:272 (Oct.) 1937.
6. Schwentker, F. F.; Gelman, Sidney, and Long, P. H.: The Treatment of Meningococcic Meningitis with Sulfanilamide, J. A. M. A. **108**:1407 (April 24) 1937.
7. McIntosh, Rustin; Wilcox, D. A., and Wright, F. H.: J. Pediat. **11**:167 (Aug.) 1937.
8. Mitchell, A. G., and Trachsler, W. H.: J. Pediat. **11**:183 (Aug.) 1937.
9. Bernstein, S. S.: J. Pediat. **11**:198 (Aug.) 1937.
10. Carey, B. W., Jr.: J. Pediat. **11**:202 (Aug.) 1937.
11. Basman, Jack, and Perley, Anne M.: J. Pediat. **11**:212 (Aug.) 1937.
12. Brennemann, Joseph: J. Pediat. **11**:238 (Aug.) 1937.
13. Pongratz, Richard: Deutsche med. Wchnschr. **63**:1015 (June 25) 1937.
14. Prontosil is the disodium salt of 4-sulfamido-phenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3', 6' disulfonic acid.
15. Willien, L. J.: Sulfanilamide Therapy in Meningococcic Meningitis, J. A. M. A. **110**:430 (Feb. 26) 1938.
16. Eldahl, A.: Lancet **1**:712 (March 26) 1938.

Marshall and his associates [17] and to those of Long [18] that sulfanilamide easily passes through the normal and inflamed meninges in about the same concentration as is found in the blood.

The present report is complementary to the original communication of Schwentker, Gelman and Long and in it will be discussed the therapeutic results obtained in seventy-two patients ill with meningococcic infections and treated with sulfanilamide alone, and the effects of combined antimeningococcus serum and sulfanilamide therapy in the treatment of thirty-four additional patients suffering from meningococcic infection.

Since the advent of sulfanilamide, 106 patients have received this drug during the treatment of meningococcic infections. For subcutaneous and intrathecal administration, a 1 per cent solution of the powdered sulfanilamide in physiologic solution of sodium chloride

TABLE 1.—*Age Incidence of Patients Treated with Sulfanilamide*

Age, Years.....	0-2	2-5	5-10	10-20	20-30	30-40	40-50	50-60
No. of patients...	12	19	18	22	20	8	3	4

is used. The solution is given intraspinally in amounts 5 cc. less than the quantity of the spinal fluid withdrawn. When given by hypodermoclysis the calculated daily dosage is administered in two divided doses at intervals of twelve hours. Hypodermoclysis is continued twice a day until the patient is able to tolerate sulfanilamide by mouth. I favor the oral administration of sulfanilamide. The drug is given in this manner unless persistent vomiting is present. In comatose patients the tablets are dissolved in water and given by nasal catheter every four hours. In the combined method of therapy serum is injected intraspinally and the same dosage of sulfanilamide given either by mouth or by hypodermoclysis. A minimum of serum is administered in an attempt to reduce the number and severity of serum reactions. I have found that only two intraspinal injections of serum are necessary in the treatment of meningitis and that usually after the first lumbar puncture the spinal fluid is sterile. At the beginning of either method of treatment with sulfanilamide a large initial dose, usually equal to the calculated daily dose, is given either by mouth or by hypodermoclysis.

The first step in the treatment of meningococcic meningitis is lumbar puncture. If the spinal fluid is cloudy and petechiae are found on examination, the treatment of meningococcic meningitis is immediately instituted. If, on the other hand, the diagnosis is doubtful a direct smear of the spinal fluid is first examined and, if gram-negative diplococci are found, the treatment is begun. Serum or sulfanilamide is given intraspinally by the gravity method. Before serum is injected, a sensitivity test to horse serum is done. In the last few cases treated with the combined method, one ampule containing 15 cc. of antimeningococcus serum was injected after drainage of the subarachnoid space. If sulfanilamide alone is used, 5 cc. less than the amount of spinal fluid withdrawn is injected intrathecally. Immediately after the first lumbar puncture, the large initial dose of sulfanilamide is offered. If, for any reason, the patient cannot take the sulfanilamide by mouth, the drug is given by nasal catheter. Only when the patient vomits is the sulfanilamide given by hypodermoclysis. Hypodermoclysis should be repeated at intervals of not more than twelve hours. The sulfanilamide medication is continued for one week. From twelve to twenty-four hours after the first lumbar puncture a second is done, at which time sulfanilamide or serum is again injected into the subarachnoid space.

I have used the same dosage of sulfanilamide in the combined method as I have in cases in which sulfanilamide alone was given. The daily dose of between 5 and 6 Gm. is rarely exceeded in adults. In infants the dosage is calculated on the basis of 250 mg. per kilogram of body weight daily. In older children the dosage is approximately 1 Gm. to 20 pounds (9 Kg.) of body weight. During the administration of sulfanilamide, fluids are restricted. In adults liquids are limited to between 1,200 and 1,500 cc. a day. The limitation of fluids, I believe, is important in maintaining a therapeutic level of sulfanilamide in the blood and spinal fluid. The state of hydration of the patient is important in determining the extent to which fluids should be limited. In addition, sodium bicarbonate is always given in the same dosage as the sulfanilamide. Acidosis is apt to occur during administration of sulfanilamide, and it is to combat acidosis that sodium bicarbonate is given. Acidosis is especially prone to occur in infants and young children, and it is in this group that the giving of sodium bicarbonate is doubly important.

Among the total number of patients treated with sulfanilamide there were nineteen deaths, a percentage of 18. Seven of the deaths occurred within twenty-four hours. Among the adequately treated patients there were twelve deaths, a case fatality rate of 12 per cent. This figure may be contrasted with a total fatality rate of 27 per cent among 368 patients treated with serum in 1935 and 1936. If the patients who died within twenty-four hours are discounted, 17 per cent of the adequately treated patients who received serum died.

TABLE 2.—*Summary of Results*

Number of Cases	Type of Treatment	Total Deaths		Twenty-Four Hour Deaths		Deaths in Adequately Treated Cases	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
72	Sulfanilamide alone	11	15.27	3	4.16	8	11.89
34	Combined sulfanilamide and serum	8	23.52	4	11.76	4	12.9
106	Sulfanilamide alone and combined sulfanilamide and serum	19	17.92	7	6.6	12	12.12
368	Serum	99	26.9	45	12.12	54	16.71

Sulfanilamide alone was used in seventy-two cases with eleven deaths, a case fatality rate of 15 per cent. There were three deaths occurring within twenty-four hours after hospitalization. When the deaths which occurred within twenty-four hours are deducted, there remain eight patients who died after receiving adequate treatment, or 12 per cent.

The combined method of treatment was instituted in thirty-four cases with eight deaths, a case fatality rate of 24 per cent. In this group there were four deaths which occurred within twenty-four hours, leaving a total of thirty adequately treated cases with four deaths, a fatality rate of 13 per cent. When this

17. Marshall, E. K., Jr.; Emerson, Kendall, Jr., and Cutting, W. C.: J. Pharmacol. & Exper. Therap. 62: 196 (Oct.) 1937.
18. Long, P. H.: Unpublished observations.

method of treatment was first used in Sydenham Hospital, eight patients were treated with four deaths. This method was then discontinued for several months, and since it has been resumed twenty-six cases have been treated with the occurrence of three deaths, two of which occurred within twenty-four hours.

In the group in which the combined method was used there were thirty-two cases in which more than one lumbar puncture was performed. Of this number there was only one case in which more than one positive spinal fluid culture was obtained. At least two lumbar punctures were done on sixty-six of the patients treated with sulfanilamide alone and from eighteen of this number more than one positive spinal fluid culture was obtained. Sixteen of this number had received sulfanilamide by hypodermoclysis throughout or at least for forty-eight hours at the beginning of the treatment. Only two of the eighteen patients had received the drug by mouth. Of those patients receiving sulfanilamide alone, forty-six had been given the drug by hypodermoclysis for at least forty-eight hours at the beginning of treatment and twenty-six were given the drug by mouth. In the group in which the drug was given subcutaneously there were nine deaths, and of those taking sulfanilamide by mouth there were only two. This would seem to indicate that giving the drug by mouth or nasal catheter every four hours was superior to the subcutaneous method of administration every twelve hours.

The concentration of sulfanilamide in the blood and spinal fluid is subject to wide variation when given by hypodermoclysis every twelve hours. At the end of the twelve hour period the sulfanilamide will usually be at a very low level, depending on the urinary output. On the other hand, in cases in which sulfanilamide is given by mouth or nasal catheter every four hours the concentration will tend to be fairly constant at what is thought to be a reasonable therapeutic level.

An attempt has been made to reduce the number of lumbar punctures in the treatment of meningitis. It was found, as already mentioned, that in very few cases was more than one positive spinal fluid culture obtained. I have noted that of all the cases in which sulfanilamide was given by mouth or by gavage every four hours, in only three were there more than one positive spinal fluid culture. Using this factor as a guide, I reduced the number of lumbar punctures, and at present only two are performed. On fifteen patients only three therapeutic lumbar punctures were performed and on fourteen only two were done. Not only does this reduce very markedly the discomfort suffered by the patient in the treatment of meningococcic meningitis but it is also very helpful from the standpoint of the time saved by the hospital attendants. The clinical course of the patient is not altered by the reduction of the lumbar punctures.

Of the total number of patients treated with sulfanilamide, blood cultures were obtained from ninety-four. Thirty-one, or 33 per cent, of this number were positive for the meningococcus. Eighteen blood cultures were obtained from the nineteen patients who died. Ten of the blood cultures obtained were found to be positive for the meningococcus, a percentage of 56.

The complications due to sulfanilamide therapy were relatively mild and infrequent in occurrence. There were three cases of hemolytic anemia and these were treated simply by stopping the drug and forcing fluids. Hemolytic anemia occurred from five days to one week after sulfanilamide medication was begun and the drug could be discontinued at that time with very little fear of the recurrence of meningococcic infection. There were two cases of sulfanilamide rash, one of which preceded the onset of the hemolytic anemia by twenty-four hours. These cases also occurred at the end of a week, at which time sulfanilamide was usually discontinued. The complications associated with meningococcic infections occurred just as frequently as in the cases in which serum therapy was used. In 368 cases in which serum therapy was used there were ten cases complicated by arthritis and two by endophthalmitis. Among the patients treated with sulfanilamide arthritis developed in five, and endophthalmitis developed in a child who had had a severe injury to the eye two weeks before there had been clinical evidence of the meningococcic infection. There were five cases of deafness occurring in the sulfanilamide treated group and only six in the 368 patients treated with serum. Of the five cases of deafness, in two the deafness was present at the time of admission before treatment was started.

There has been a reduction in the number of recurrences since the introduction of sulfanilamide in the treatment of meningococcic infections. There was only one recurrence in the 106 cases here reported, and in this case sulfanilamide per se was not given but one of the derivatives. On readmission this patient did very well when treated with sulfanilamide alone and recovered very rapidly. Of the 368 serum treated patients there were six recurrences.

RESULTS

1. There were 106 patients with meningococcic infection treated at Sydenham Hospital with nineteen deaths, a fatality rate of 18 per cent. The case fatality rate in the adequately treated group was 12 per cent.

2. When sulfanilamide alone was used the fatality rate was 15 per cent. In the adequately treated cases, the fatality rate was 12 per cent.

3. The combined method of treatment was used in thirty-four cases with a case fatality rate of 24 per cent. The fatality rate in the adequately treated group was 13 per cent. Among the last twenty-six patients treated in this manner there were three deaths, two of which occurred within twenty-four hours.

4. The spinal fluid cultures were more consistently sterile after from twelve to twenty-four hours of treatment in those cases in which sulfanilamide was taken every four hours by mouth or by nasal catheter rather than when given every twelve hours by hypodermoclysis.

5. The number of lumbar punctures in the treatment of meningitis has been markedly reduced.

6. The complications due to sulfanilamide therapy were infrequent and very mild. The number of recurrences were reduced. Those complications due to meningococcic infections were not significantly reduced in occurrence.

CONCLUSION

Since the introduction of sulfanilamide in the treatment of meningococcic infection there has been a definite decrease in the number of deaths, not only in the adequately treated but also in those fulminating cases which usually terminate fatally within twenty-four hours. The discomfort suffered by the patient directly due to the treatment is lessened owing to the simplification of the treatment, and the hospital stay has been notably reduced.

Harford Road at Herring Run.

COMBINATION COURSES OF BISMUTH ADMINISTRATION

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Intramuscular bismuth therapy against syphilis ranges between the extreme of very slow absorption from the oil suspensions of compounds that dissolve very slowly in water, such as the subsalicylate, and the other extreme of the relatively rapid absorption from watery solutions. With the watery solutions an effective concentration of bismuth in the blood and tissues is reached in a short time, perhaps after a single injection. As the excretion of these solutions is also more rapid, their action is relatively brief and they must be administered more frequently. The oil suspensions have the advantage that they may be given at longer intervals. They tend to become cumulative when injected once a week. The effective concentration in the blood is therefore approached more slowly, probably only after from two to four weeks. These extremes are bridged by a variety of bismuth preparations, such as oil suspensions of more soluble compounds and the oil-soluble compounds. It occurred to us that it might be advantageous to approach the problem in a different way, namely by an interlocking sequence of watery solutions and salicylate suspensions, adjusted to build up an effective concentration rapidly by use of the watery solution and a continuous concentration meanwhile by use of the salicylate suspension, the injections of the watery solution being graded off as the salicylate concentration rises. The course as projected consisted of ten weekly injections of an oil suspension of bismuth subsalicylate supplemented at the beginning by six injections of a soluble compound, three in the first week, two in the second week, one in the third week and none thereafter.

In one series the subsalicylate was given in the usual weekly dose: 1 cc. of a suspension in olive oil, which contained 0.13 Gm. of bismuth subsalicylate, or 75 mg. of bismuth. In another series double this dose, 2 cc., 0.26 Gm. of bismuth subsalicylate, or 150 mg. of bismuth, was employed. For the water-soluble compounds we chose iodobismitol and sobisminol, because their absorption rate is rapid while their excretion is less fugacious than that of the bismuth thioglycollate. The iodobismitol is a solution of 6 per cent sodium iodobismuthite and 12 per cent sodium iodide in propylene glycol. The intramuscular dose is 2 cc., equivalent to approximately 25 mg. of bismuth. Sobisminol is a true solution of 3 per cent sodium bismuthate, 8 per cent tri-isopropanolamine and 50 per cent propylene glycol, the remainder being water. The dose used was 2 cc. per injection, 60 mg. of sodium bismuthate, or approximately 40 mg. of bismuth. This resulted in the following experimental courses (the doses being given in milligrams of bismuth for each injection):

1. Bismuth subsalicylate 0.13 Gm., 75 mg. of bismuth
2. Bismuth subsalicylate 0.26 Gm., 150 mg. of bismuth
3. Iodobismitol 2 cc., 25 mg. of bismuth
4. Iodobismitol 2 cc., 25 mg. of bismuth, plus bismuth subsalicylate 0.13 Gm., 75 mg. of bismuth
5. Iodobismitol 2 cc., 25 mg. of bismuth, plus bismuth subsalicylate 0.26 Gm., 150 mg. of bismuth
6. Sobisminol 2 cc., 40 mg. of bismuth

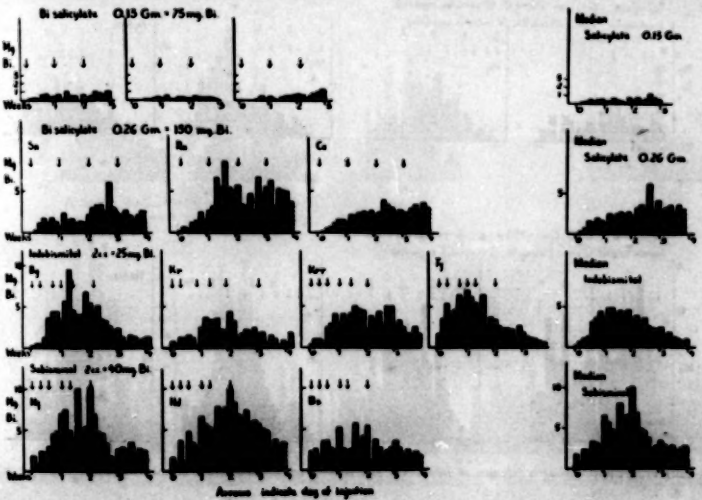

Chart 1.—Daily urinary excretion after injections of (*a*) bismuth subsalicylate 0.13 Gm., (*b*) bismuth subsalicylate 0.26 Gm., (*c*) iodobismitol 2 cc. per injection and (*d*) sobisminol 2 cc. per injection.

This work was supported by grants from the Council on Pharmacy and Chemistry of the American Medical Association.
Read before the Section on Dermatology and Syphilology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.
From the Department of Pharmacology and the Department of Dermatology and Syphilology, Western Reserve University School of Medicine, and City and University hospitals.

7. Sobisminol 2 cc., 40 mg. of bismuth, plus bismuth subsalicylate 0.13 Gm., 75 mg. of bismuth

8. Sobisminol 2 cc., 40 mg. of bismuth, plus bismuth subsalicylate 0.26 Gm., 150 mg. of bismuth

Three or four patients were used for each course, with daily determination of the urinary excretion of bismuth. The curve for each patient is shown in charts 1, 2 and 3, as is the median for each group. For simplicity the median curves were smoothed and projected by extrapolation, for the determinations were not continued after four weeks because of the difficulty of longer hospitalization of patients.

IODOBISMITOL AND BISMUTH SUBSALICYLATE

The results are shown in chart 4. The upper set of curves shows (*a*) the slowly ascending curve when bismuth subsalicylate alone is injected and the dose is 0.13 Gm. (75 mg. of bismuth) weekly. The average level of urinary excretion of 1 mg. of bismuth a day is reached in three weeks and 2 mg. of bismuth a day probably in six weeks. With iodobismitol alone (*b*) by a gradually descending sequence of doses, i. e. three the first week, two the second week, one the third week and none thereafter, the maximum of the excretion curve is reached in about ten days, at 4.5 mg. of bismuth a day. It would have fallen to the 2 mg. level about the end of the third week and below 1 mg. in the fourth week. The sum of the two curves would give the dotted curve (*c*), which is only slightly higher than the curve for iodobismitol alone for the first two weeks but then falls and keeps practically horizontal at about 2 mg. of bismuth a day until it fuses with the ascending salicylate curve at the seventh week. The actual excretion happens to ascend somewhat more slowly, but to about the same level (5 mg. of bismuth a day), after which its course is practically identical with the arithmetical sum.

The lower set of curves shows (*a*) the excretion after bismuth subsalicylate 0.26 Gm. (150 mg. of bismuth), which reaches a considerably higher level, 2 mg. by the end of the first week and probably 4 mg. in the sixth week. Adding this curve to the curve for iodobismitol (*b*), which is identical with that in the upper figure, gives the sum shown in the dotted curve, *c*. This curve ascends gradually to a maximum of 6 mg. at the end of the fourth week and then falls to unite with the salicylate curve at the end of the fifth week, with a level a little above 3 mg. The actual curve runs higher at first, reaching 10 mg. at the end of the second week, and then descends to join the theoretic curve at the sixth week.

SOBISMINOL AND BISMUTH SUBSALICYLATE

For sobisminol and bismuth subsalicylate the curves are shown in chart 5, the upper group being for the 0.13 Gm. dose of salicylate (75 mg. of bismuth) and the lower group for the 0.26 Gm. dose (150 mg. of bismuth). The curves for the subsalicylate are the same as those in chart 4. The curve for sobisminol alone (*b*), in the descending doses which were used, reaches its maximum at a level of 7 mg. of bismuth about the end of the second week and descends gradually to about 2 mg. at the end of the fourth week and below 1 mg. at the sixth week. The sum of the two curves (*c*) is but little higher than that of sobisminol alone during the first two weeks, but the descent joins the ascending curve of the salicylate in the sixth week and thus remains above 2 mg. The actual curve for the combined medication (*d*) is practically identical with the theoretic curve.

When the curve for sobisminol is added to the curve for salicylate in the higher doses, as shown in the lower set of curves (*c*), the excretion reaches the maximum of 10 mg. of bismuth at the end of two weeks, falls to about 5 mg. by the end of the fourth week and keeps at this level until it joins the ascending curve there at about the end of the seventh week. The actual curve (*d*) runs somewhat higher.

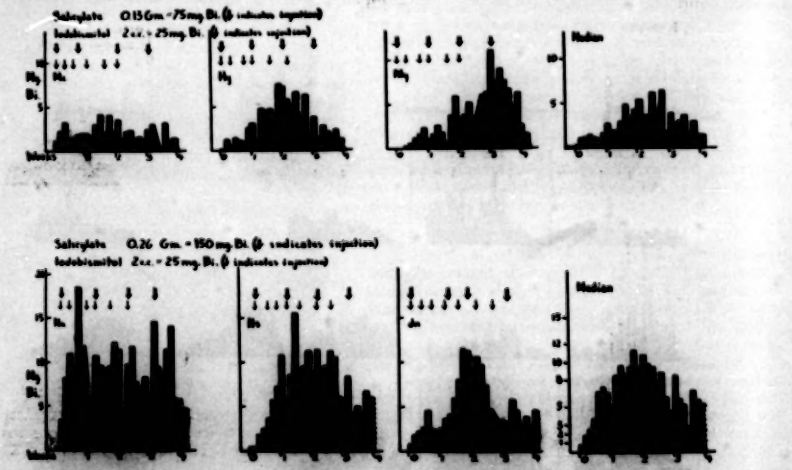

Chart 2.—Daily urinary excretion after injection of iodobismitol plus bismuth subsalicylate 0.13 Gm. and iodobismitol plus bismuth subsalicylate 0.26 Gm.

The variation between the theoretic and the actual observations for the combination are probably not significant. The significant fact is that the combination attained a high excretion level in two weeks, which fell gradually to join the ascending salicylate curve in from five to seven weeks.

With the combination, therefore, the excretion from the very start is materially higher than that which is attained by salicylate alone after from five to seven weeks of administration; namely, 2 mg. of bismuth for the lower dose, 0.13 Gm. (75 mg. of bismuth), and 4 mg. for the higher dose, 0.26 Gm. (150 mg. of bismuth). During the initial two weeks, however, the excretion curve reaches a median of 5 mg. of bismuth with iodobismitol plus salicylate 0.13 Gm., from 6 to 10 mg. with iodobismitol plus salicylate 0.26 Gm., 9 mg. with sobisminol plus salicylate 0.13 Gm. and 12.5 mg. with sobisminol plus salicylate 0.26 Gm. It is reasonable to assume that this initial intensive medication should be useful for an intensive effect on the spirochetes, which would be maintained when the dose fell to the safer but still effective levels of the ascending salicylate curves. None of the patients showed any toxic effects, nor would these be expected, because the high concentrations are not continued for any length of time. We may add that the 0.26 Gm. dose of salicylate has been used in other cases for the whole course without toxic results.

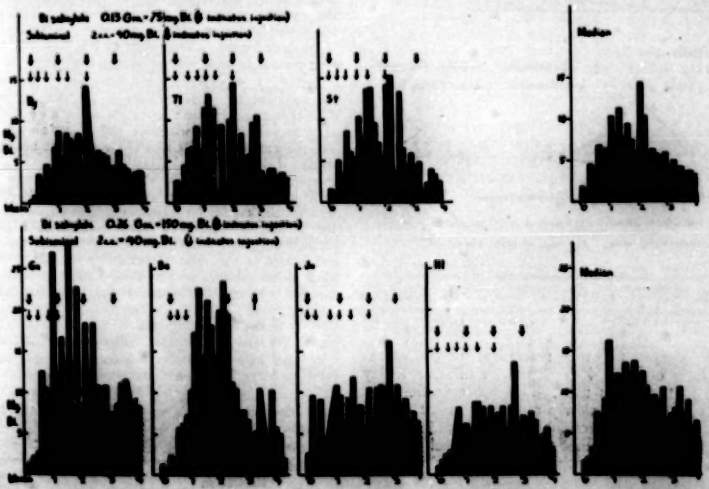

Chart 3.—Daily urinary excretion after injection of sobisminol plus bismuth subsalicylate 0.13 and sobisminol plus bismuth subsalicylate 0.26 Gm.

CLINICAL COMMENT

One of the problems with bismuth therapy for syphilis is to achieve a rapid rise of the metal in the blood stream to a therapeutic level and to keep it there without too great hardship on the patient. This can be achieved by biweekly or triweekly intramuscular injections of certain water-soluble bismuth compounds, but what patient will consent to such frequent injection for ten or twelve weeks at a stretch, even if he can afford them? It is well known that eventually certain of the insoluble bismuth salts, if they have been injected enough times, will reach a therapeutic level in the blood stream. If some combination can be added to this slowly rising bismuth curve that will raise the level within a day or so and hold it long enough so that it may gradually grade off into the rising level from the bismuth subsalicylate, the problem will be solved. This we believe we have achieved by the combined use of iodobismitol or sobisminol and weekly injections of bismuth subsalicylate. The accompanying table illustrates our point.

Such a form of bismuth therapy would be particularly useful in the acute stage of syphilis when the patient is sensitive to arsenic and it is necessary to rely on other antisyphilitic measures. Moreover, for the patient with early syphilis who is just starting therapy, this schema might be employed in the first course of bismuth therapy when the clinician is desirous of dealing a heavy blow to the spirochetes from another angle than that of arsenic. Again, it would be most useful for the patient who is sensitive to arsenic and has for example syphilitic meningitis. In certain cases the clinician would find the bismuth subsalicylate in 1 cc. doses (0.13 of bismuth) sufficient. Certainly for robust males this drug in 2 cc. doses could be employed. With this combined bismuth therapy the somewhat

Schema of Combination Bismuth Treatment

Weeks of Heavy Metal Treatment						
First	X or X¹	plus	Y	Y	Y	or Z Z Z
Second	X or X¹		Y	Y		Z Z
Third	X or X¹			Y		Z
Fourth	X or X¹					
Fifth and so forth	X or X¹					

X—bismuth subsalicylate, 1 cc. (0.130 Gm. of bismuth).
X¹—bismuth subsalicylate, 2 cc. (0.260 Gm. of bismuth).
Y—iodobismitol, 2 cc. (0.025 Gm. of bismuth).
Z—sobisminol, 2 cc. (0.040 Gm. of bismuth).

more irritating injections of water-soluble bismuth preparations would gradually be supplanted by the comparatively painless medication with bismuth subsalicylate.

SUMMARY AND CONCLUSIONS

A graded sequence of injections of soluble bismuth preparations (iodobismitol and sobisminol) with continued weekly injections of bismuth salicylate produces a high initial concentration of bismuth as reflected in

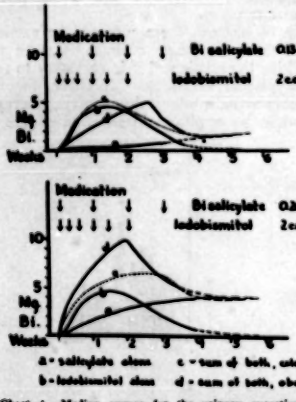

Chart 4.—Median curves for the urinary excretion of bismuth after injection of bismuth subsalicylate (a), iodobismitol (b) and bismuth subsalicylate plus iodobismitol (d). The presumptive further course is indicated by broken lines. The dotted lines (c) represent the arithmetical sum obtained by adding the two curves a and b. The upper set of curves gives results after salicylate 0.13 Gm. and the lower set after salicylate 0.25 Gm.

the urinary excretion, which reaches at the end of two weeks a level of from 4 to 12 mg. of bismuth a day, according to the drugs used. This concentration then falls so as to join the slowly ascending curve characteristic of salicylate injections about the end of from five to seven weeks, so that the median level does not fall below 2 mg. of bismuth for the lower dose (0.13 Gm.) of salicylate and 4 mg. of bismuth for the higher dose (0.26 Gm.) of salicylate. The sequence therefore secures the benefit of the intensive action of the water-soluble bismuth preparations in the early part of the course and the advantages of the convenience of salicylate injections in the latter part of the course.

This form of combined bismuth therapy is offered for use in the treatment of patients with acute syphilis who are sensitive to arsenic when a rapid but prolonged effect of bismuth is called for. It may also be profitably employed as the form of bismuth medication in the treatment of early syphilis.

ABSTRACT OF DISCUSSION

Dr. George V. Kulchar, San Francisco: The paper of Drs. Sollmann and Cole and their associates is a happy compromise, I think, between the two camps existing at present, those who advocate a soluble bismuth compound and those who believe an oil suspended bismuth to be more logical. I think the compromise evoked utilises the best features of each. When it comes to bismuth, we are somewhat in a state of flux, perhaps induced by several questions. We do not know exactly what we desire therapeutically from a bismuth compound. In other words, is the spirocheticidal effect directly proportional to the absorbed dose, as it would seem from animal experimentation, or should one take the other view, that the bismuth perhaps in combination with some protein acts as a catalyst or a spirochetostatic agent? The second question which leads to indecision is Does urinary excretion truly measure bismuth effect? In others words, is the number of milligrams of bismuth excreted daily in the urine a mathematical expression of the spirocheticidal effect? Another question which causes trouble along the same line is Can bismuth be accurately measured in the blood stream? The order of magnitude of bismuth determinations to a large degree makes the practicing syphilologist wonder whether it is an accurate index of absorption. If the concept is accepted that the spirocheticidal effect is directly proportional to the urinary excretion of bismuth, the method advocated by Dr. Cole and his associates affords rapid approach in the treatment of syphilis, particularly in the cases that they mentioned, and I might add in early syphilis in elderly patients to whom one hesitates sometimes to give an arsphenamine. So far as bismuth salicylate is concerned, this is one means of initiating treatment. The same effect may be obtained by the use of either one of the two soluble compounds mentioned by the authors, sobisminol and iodobismitol. The more rapidly absorbable and consequently excreted compounds seem to me to be more logical. Compounds of this type may be given over long periods of time without cumulative effects on toxicity.

Dr. P. J. Hanzlik, San Francisco: My colleagues at Stanford and Dr. J. R. Scholtz of Los Angeles have sufficient clinical data on bismuth salicylate to indicate that it is inefficient because it is an insoluble and poorly absorbed compound, and the authors' results also show that the absorption is very small. I believe I understand why a bismuth compound of that kind is chosen. It is retained for a long time in the body and assumed there is a continuous bismuth streaming through the tissues for sustained action on the syphilitic virus. But it may be questioned whether there is a continuous, or at least adequate, bismuth streaming through the tissues when one considers the poor absorbability of this product and the local tissue reaction to it. This product is walled off in the muscles and can be found at the injection site for weeks,

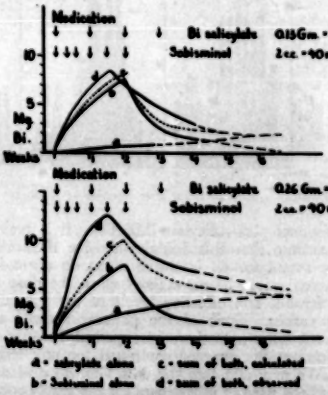

Chart 5.—Median curves for the urinary excretion of bismuth after injection of bismuth subsalicylate (a), sobisminol (b) and bismuth salicylate plus sobisminol (d). The presumptive further course is indicated by broken lines. The dotted lines (c) represent the arithmetical sum obtained by adding the two curves a and b. The upper set of curves gives results after salicylate 0.13 Gm. and the lower set after salicylate 0.26 Gm.

months and sometimes even years. Soluble compounds of bismuth are unquestionably superior to the insoluble. I agree with the authors that iodobismitol and sobisminol may be placed somewhere between the most soluble and the least soluble bismuth compounds and produce the desired result so far as the concentration of bismuth and action in the tissues are concerned. The time period for disappearance of the virus

from syphilitic lesions and their healing is inversely proportional to the dosage; in other words, the higher the dosage or the higher the concentration in the tissues, the faster are the clearing and healing of the lesion. The urinary excretion of bismuth is the simplest and most practical guide to the efficiency of medication, much as one would like to have more direct control of the bismuth content of tissues and blood. We have introduced a short clinical method for estimating bismuth in urine, which can be readily applied by an office, technical or clinical assistant. It provides a fairly good chemical control on the treatment. Since insoluble products are much less efficient and desirable, may I suggest the use of an oral bismuth compound, in an exclusive bismuth system, for more efficient and sustained effects and greater convenience? I don't know what the authors think about this, but the oral sobismінol is definitely effective in syphilis. I appreciate the objections to oral medication in the treatment of syphilitic patients, but, aside from the toxicity of arsenicals and mercurials, most of these are not valid and will disappear when there is a better appreciation of the possibilities for bismuth. As for toxicity and possible injuries to viscera, blood and other undesirable effects, sobismінol is not comparable with acetarsone or mercury, whether sobismінol is taken by the patient himself or given under the supervision of a physician.

DR. BEN A. NEWMAN, Los Angeles: It is well known that the most frequent untoward reaction and complaint, especially by patients in private practice, concerns the deposition of bismuth in the gum margins. Have the authors observed any increase in the incidence of gingivitis or stomatitis with this sustained elevation of bismuth in the blood stream?

DR. JOSEPH GRINDON, St. Louis: The advocacy by the authors of the combined use of these two preparations in early syphilis is convincing, but I ask whether in late or latent syphilis, and in the absence of any immediately threatening lesion, it presents any advantage.

DR. HARRY M. ROBINSON, Baltimore: I should like to ask the authors about dermatitis reactions caused by injections of this bismuth compound of 2 decigrams a week. Quite a few cases of dermatitis are found in our clinic. They are of the lichenoid or eczematous types, not exfoliative but still very annoying. I should like to know whether with this high concentration of bismuth the dermatitis is of any more or less frequent occurrence.

DR. ELMORE B. TAUBER, Cincinnati: Before the insoluble preparations of bismuth are relegated to the background and either the oral administrations or the soluble ones are adopted, I want to make a plea for bismuth subsalicylate if it is placed in the proper vehicle. Unfortunately the vehicles that have been placed on the market have been mineral oils and other oils which are the ones when deposited intramuscularly that act as a foreign body and cause a fibrosis with a consequent lowering of the amount of bismuth absorbed. In the last five or six years I have used a preparation of bismuth subsalicylate incorporated in a vegetable compound which is simple, easy to make, with no pain resulting, and this compound is nothing but Crisco, which has stearin in it and which is absorbed easily; and shortly afterward, not within twenty-four to forty-eight hours but within a week, the excretion of from 2 to 3 mg. of bismuth in the urine is observed. It is inexpensive, painless and equal to or better than any preparation that I know on the market. I should also like to ask whether the authors have had any use of oral bismuth.

DR. HAROLD N. COLE, Cleveland: Naturally, one would hesitate to employ dosages of bismuth that would continuously cause an excretion of 15 mg. of metallic bismuth a day in the urine. To Dr. Grindon I will say that this is designed principally for acute syphilis or situations in which a rapid bismuth effect is desired. I do not think it is indicated in late syphilis or for old syphilitic patients but in these acute cases. We have not seen any bad effects from this therapy in the limited number of cases in which we have employed it. Naturally, patients who are getting a dosage of this sort should be watched closely. Probably the first symptom that one would note would be a bismuth line. It is true that once in a while one encounters a dermatitis from bismuth, but it is uncommon, nothing like the frequency that is encountered with preparations of the arsphenamines that are on the market. With regard to Dr. Tauber's notation about Crisco, a Cincinnati-made product, I would say that we have not used it but that, as he knows, all suspensions of bismuth that are on the market today are in vegetable oils; mineral oils are not employed any more. The reason we are suggesting this type of therapy is that with the water soluble preparations one does get a certain amount of irritation and discomfort, and while it may be justifiable for one or two or three weeks while one is anxious to get them under control, it probably would not be possible to get these patients to continue coming in twice a week for a comparatively irritating preparation as compared to the effects of bismuth subsalicylate. On that account we feel that it would be preferable to change over gradually to this other compound. I should like to say that sobismінol has given the highest excretion of bismuth in the urine of any preparation that we have worked with. We have used this preparation some by mouth in a form that Dr. Hanzlik has worked out. It seems as though from our limited experience there is little or no discomfort from its oral use, and one gets an excretion that compares well with that of iodobismitol. We have had insufficient experience, however, to give any final results on it.

DIMENSIONS OF THE RED CELLS IN FAMILIAL HEMOLYTIC ANEMIA

WITH PARTICULAR REFERENCE TO ATYPICAL CASES

JOSEPH M. HILL, M.D.
DALLAS, TEXAS

Repeated complete measurements of the red cells have been made in seven cases of familial hemolytic anemia studied in Baylor University Hospital during the past two years. The results permit some definite conclusions with regard to the diagnostic value of the size and shape of the erythrocytes (spherocytosis). Furthermore, changes in these dimensions during the course of the disease have been studied in relation to clinical variations, onset of crisis, erythropoiesis and splenectomy. Interpretation of the modifications of corpuscular size and form is based on determination of the normal range of these qualities and consideration of pathologic factors known to affect them.

Alteration of the dimensions of the red cells in familial hemolytic anemia has been recognized almost as long as the disease entity itself. Chauffard [1] in 1907 first noted the decreased diameter, subsequently regarded as the chief characteristic by most writers, including Naegli,[2] Dawson [3] and Haden.[4] Increased thickness and decreased diameter were said by Naegli to be the fundamental inherited feature of the disease. Gänsslen [5] first related this change in shape to increase in fragility. Meulengracht [6] and von Boros [7] expressed

From the Department of Pathology, Hospital Laboratory Division, Baylor University College of Medicine.
Read before the Section on Pathology and Physiology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Chauffard, M. A.: The Pathogenesis of Congenital Icterus in Adults, Semana méd. 27:1: 25, 1907.
2. Naegli, Otto: Blutkrankheiten und Blutdiagnostic, ed. 5, Berlin, Julius Springer, 1931, p. 292.
3. Dawson, B. E.: Hume Lectures on Haemolytic Icterus, Brit. M. J. 1:921-928 (May 30) 1931, 963-966 (June 6) 1931.
4. Haden, R. L.: The Mechanism of the Increased Fragility of the Erythrocytes in Congenital Hemolytic Jaundice, Am. J. M. Sc. 188:441-449 (Oct.) 1934.
5. Gansslen, M.: Ueber hamolytischen Ikterus deutschen, Arch. f. klin. Med. 140:210-226 (Sept.) 1922.
6. Meulengracht, E.: Der chronische heriditäre hämolytische Ikterus, Leipzig, Dr. Werner Klinkhardt, 1922.
7. von Boros, J.: Ueber gross, Volumen und Form der menschlichen Erythrocyten und deren Zusammenhang; II. Die Microcytose beim hamolytischen Ikterus, Wein. Arch. f. ins. Med. 11:255 (Feb.) 1926.

the opinion that spherocytosis is not a specific feature of familial icterus but a regeneration phenomenon unrelated to fragility.

Von Boros [8] and Haden [9] assumed the red cell to be a cylinder for purposes of calculation and expressed the volume-thickness relationship by an index. Haden presented conclusive experimental evidence that there

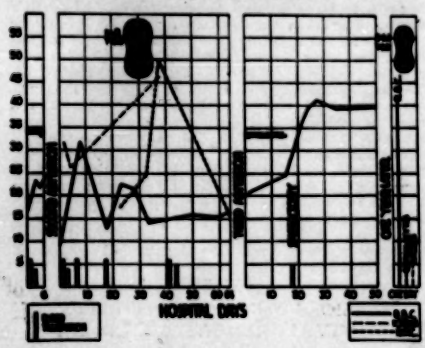

Chart 1.—Progress of the disease in case 1. Read the values for the reticulocytes and the icterus index directly from scale. For the red cell count shift the decimal one place to the left (divide by 10) and read in millions.

is a direct relationship between the degree of approach to sphericity as expressed by this index and the fragility of the red cells and stated that microspherocytosis is the fundamental variation from normal, all other phenomena of the disease being secondary. Castle [10] confirmed this mechanism of fragility and ruled out differences in osmotic behavior as a possible factor. He also devised an absolute rather than a relative index of sphericity, expressing as a percentage the difference between the corpuscular volume and the volume of a sphere of equal surface.

The primary role of the spleen in this disease has been upheld by many hematologists. Doan, Curtis and Wiseman [11] in 1935 recognized spherocytosis but found that the erythrocytes approached the normal form after splenectomy. Vaughan [12] suggested that both erythropoiesis and splenic function are at fault but stated that spherocytosis is not the fundamental abnormality.

Momigliano-Levi and Bairati [13] expressed the opinion that the bone marrow can produce normal cells when relieved of the excessive load of increased destruction in the spleen.

Josephs [14] suggested that an antihemolytic substance normally present to maintain the equilibrium between erythropoiesis and destruction may be absent in sickle cell anemia and hemolytic jaundice.

8. von Boros, J.: Die Behandlung der Anamien, Ergebn. d. inn. Med. u. Kinderh. **43**: 635-740, 1932.

9. Haden, R. L.: The Volume Thickness Index of the Erythrocyte of Man, J. Lab. & Clin. Med. **20**: 567-571 (March) 1935.

10. Castle, W. B., and Deland, G. A.: Susceptibility of Mammalian Erythrocytes to Hemolysis with Hypotonic Solutions, Arch. Int. Med. **60**: 949-966 (Dec.) 1937.

11. Doan, C. A.; Curtis, G. M., and Wiseman, B. K.: The Hemolytopoietic Equilibrium and Emergency Splenectomy, J. A. M. A. **105**: 1567-1574 (Nov. 16) 1935.

12. Vaughan, J. M.: Red Cell Characteristics in Acholuric Jaundice, J. Path. & Bact. **48**: 561-577 (Nov.) 1937.

13. Momigliano-Levi, G. M., and Bairati, A.: Distribution of Erythrocyte Population in Regard to Diameters and Osmotic Resistance in Splenectomized Cases of Hemolytic Icterus: A Contribution to an Understanding of the Pathogenesis of the Disease, Am. J. M. Sc. **190**: 610-617 (Nov.) 1935.

14. Josephs, H. W.: Studies in Hemolytic Anemia. II. The Presence of an Anti-Hemolytic Factor in Human Plasma, Bull. Johns Hopkins Hosp. **63**: 53-69 (Jan.) 1938.

Since the validity of the results reported in this series of cases depends on the technic employed, a brief statement of method is essential.

METHOD

In determining complete dimensions of the erythrocytes, the red cell count, the mean cell diameter and the percentage of packed cells (hematocrit) must be obtained. Simultaneous determination of the hemoglobin is also desirable.

In enumerating the red cells all known precautions with regard to the use of certified equipment, proper shaking and the counting of a large number of cells were observed. Blood was taken from the same sample as that examined with the hematocrit, and 320 small squares were counted.

The mean cell diameter was obtained by a modification of the technic of Price-Jones.[15] The corpuscles were projected at a magnification of exactly 3,000 diameters onto a white target and were measured by fitting to the images circles drawn to a proper scale on white cards. An effective numerical aperture of 1.30 gave full resolution. At least 500 cells were measured in each instance.

For hematocrit determinations Magath tubes were used throughout, and in the later cases duplicate determinations with Wintrobe tubes were also made. Heparin was used as an anticoagulant, but in the duplicates 1.4 per cent sodium oxalate was employed with identical results. All specimens were centrifuged for at least one hour at a minimum speed of 2,500 revolutions a minute. Constant red cell volume was always obtained under these conditions in later experiments. Increasing the speed of centrifugation to 4,500 revolutions showed no significant change in the packing of the red cells.

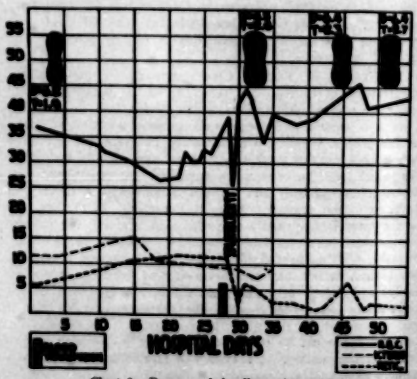

Chart 2.—Progress of the disease in case 2.

Only rarely can all the diagnostic criteria of familial hemolytic anemia be found in one case. In the present study diagnosis was based on several considerations. First, the familial character was considered established if undoubted spherocytosis was found in other members of the family or if a sufficiently definite history of splenomegaly, anemia or jaundice was obtained. Second, the hemolytic character of the anemia was determined

15. Price-Jones, Cecil: Red Blood Cell Diameters, New York, Oxford University Press, 1933.

by a study of the state of equilibrium between production and destruction of red cells, indicated by use of laboratory procedures as outlined in the exhibit.[16] Third, repeated measurement of the red cells with the finding of spherocytosis, microcytosis or both on at least one occasion was regarded as most important. Finally, confirmation of the diagnosis was often made

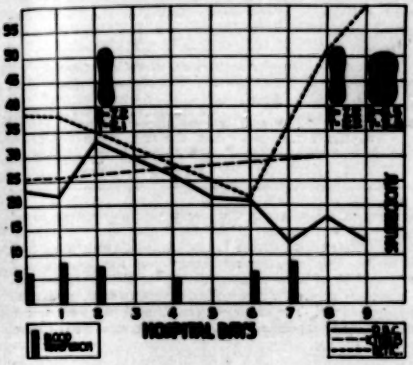

Chart 3.—Progress of the disease in case 3.

possible by examination of the spleen, by the clinical course before and after splenectomy or, in the event of death, by postmortem examination. Studies of the sternal marrow were also employed, particularly in ruling out leukemia.

In expressing corpuscular shape in terms of its approach to spherical form, neither Haden nor Castle reported the limits of physiologic range. Because the biconcave form of the red cell is well adapted to changes in volume and osmotic variations in the blood are known to be accompanied by a shift of water across the red cell membrane, definite alteration in erythro-

TABLE 1.—*Measurements of the Red Cells, Case 1* *

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
30	186	8	3.8	35	1.73
1 year later	90	6.4	2.8	36.3	1.7

* Note that the lower the value of Castle's index, the greater the sphericity, whereas in the case of Haden's index the reverse is true. In the tables M.C.V. indicates mean corpuscular volume; M.C.D., mean corpuscular diameter; M.C.T., mean corpuscular thickness; Castle's index, Castle's absolute index of sphericity, and Haden's index, Haden's volume-thickness index.

cytic form must occur. In the first fifteen normal persons of a series now being studied, this variation was borne out. The volume-thickness index ranged from 0.95 to 1.4 with a mean of 1.18, and the absolute index of sphericity varied from 46.4 to 68.6 with a mean of 57.6. The former differs by a significant amount from Haden's normal value of 1, while the latter, because of the greater numerical range, is in practical agreement with Castle's normal value of 59. In addition, similar physiologic variations were found in the same person at different times, for example after exercise.

16. Hill, J. M., and Waters, Lewis: Hematologic Exhibit: IV. The Diagnosis of Hemolytic Anemia, A. M. A. Meeting, San Francisco, June 1938. Scientific Exhibit at the Eighty-Ninth Annual Session of the American Medical Association.

Although Price-Jones, Vaughan and Goddard[17] studied the diameter, volume and thickness of the red cells in 100 normal persons, no calculation of sphericity was made. Their mean diameter of 7.17 microns, however, did not differ significantly from our mean of 7.02 microns. Furthermore, calculation of sphericity from their limits of diameter and volume indicate a possible range as great as ours. Consequently in the series of cases herein reported values above 1.5 for volume-thickness index or below 45 for Castle's absolute index were regarded as definite evidence of spherocytosis.

TABLE 2.—*Measurements of the Red Cells, Case 2*

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
4	89	6.1	1.9	35.7	1.3
21	90	6.3	2.6	41.4	1.6
45	75	6.4	2.3	47	1.4
80	92	6.4	2.7	38	1.7

Values near the limit of normal were looked on with suspicion, especially with small diameters or marked variation in apparent thickness in the smears.

CASE 1.—K. M., a white boy aged 7, had the acute febrile type of hemolytic anemia, with macrocytosis followed by clinical cure and microcytosis after splenectomy, as illustrated in chart 1. Clinical study showed jaundice, anemia and a palpable spleen. A family history of jaundice was established. The measurements of the red cells are listed in table 1.

CASE 2.—J. T. B., a white boy aged 12, had a moderately severe type of red cell destruction, with clinical features of slight jaundice, splenomegaly, hepatomegaly and an unhealed chronic ulcer of the leg. Hemolytic icterus in his mother was verified by postmortem examination. Chart 2 illustrates the progress of the disease and the response to splenectomy, and table 2 shows the successive dimensions of the red cells.

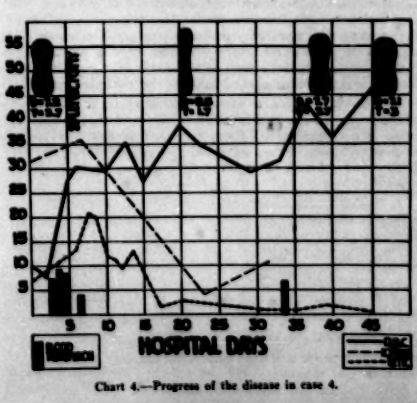

Chart 4.—Progress of the disease in case 4.

CASE 3.—M. C., a white girl aged 14, had an acute hemolytic crisis, as demonstrated in chart 3. No significant family history could be discovered. Clinical study disclosed transient neurologic symptoms, including hemiplegia and paralysis of the left arm. There were pallor, icterus and bleeding gums. The spleen was not palpable. The series of red cell measurements is given in table 3. Death occurred a few hours after splenectomy. Postmortem examination showed peculiar hyaline thrombi in a large number of the smaller vessels of all the sections examined,

17. Price-Jones, Cecil; Vaughan, J. M., and Goddard, H. M.: Normal Hematologic Standards, J. Path. & Bact. 40:503-519 (May) 1935.

including sections of the heart, brain, liver and spleen. The spleen was otherwise characteristic of familial hemolytic anemia.

Case 4.—A. T., a white woman aged 54, had slight jaundice, scanty urination, weakness, dyspnea and fever. The spleen was not palpable. A significant family history was demonstrated only through examination of her son's corpuscles. The acuteness of the hemolytic crisis as well as the favorable effect of

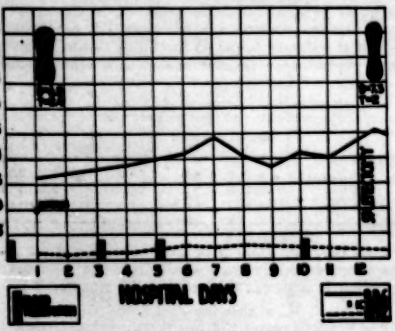

Chart 5.—Progress of the disease in case 5.

splenectomy is easily seen in chart 4. The spleen showed the characteristic enlargement and microscopic picture. The corpuscular dimensions are shown in table 4.

Case 5.—H. B. W., a white man aged 25, a brother of patient 6, had had previous attacks of anemia, jaundice and splenomegaly. Clinical investigation showed marked enlargement of the spleen and liver, general anasarca and extreme pallor. The results of laboratory tests are given in chart 5 and the complete measurements of the red cells in table 5. The patient refused splenectomy until he felt definitely worse. He died twelve hours after operation. The spleen differed from that in the other cases only in being larger and more heavily loaded with hemosiderin and in showing slight fibrosis. Postmortem examination showed enlargement of the liver with lobular cirrhosis, bronchopneumonia and early diffuse peritonitis.

Case 6.—B. M. W., a white youth aged 19, a brother of patient 5, had an identical history and the same clinical appearances. The course of the illness is shown in chart 6. During the first admission, which antedated that of his brother, definite microcytosis and moderate spherocytosis were apparent, as shown

Table 3.—*Measurements of the Red Cells, Case 3*

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
2	80.5	7.2	2.17	59	1.19
5	98.4	7.9	2.2	56	1.23
9	131	6.55	3.8	28.5	2.83

in table 6. At the second admission, one year later, with the anemia much worse a definite macrocytic tendency was apparent, with abnormal thinness of the red cells. Gastric analysis gave negative results, and leukopenia was present. The white cell count varied from 3,400 to 1,350 during this admission. After failure of transfusion and intramuscular administration of liver extract to arrest his progressive anemia, two doses of 20 cc. of liver extract were given intravenously in an attempt to unmask the possible complicating macrocytic factor of cirrhosis of the liver and to remove any inhibition of erythrocytic maturation. The dramatic response of the reticulocytes, shown in chart 6, was accompanied by progressive reduction in the diameter of the cells, with a slight increase in thickness and fragility but with no improvement of the anemia. Transfusion was of no avail, and the increased destruction of erythrocytes was reflected in the increased icterus index. Splenectomy was recommended again but was refused, and the patient returned home to die two weeks later. The diagnosis was familial hemolytic anemia complicated by cirrhosis of the liver giving a clinical picture identical with Banti's syndrome.

Case 7.—J. B. A., a white man aged 60, an outpatient, had had intermittent episodes of splenomegaly, anemia and sometimes jaundice since the age of 10. In the five years during which he was under observation, the anemia was only moderate, with the red cell count varying between 3,800,000 and 4,400,000 and the percentage of reticulocytes from 7 to 11. The red corpuscles were constantly microcytic, with an average mean cell

Table 4.—*Measurements of the Red Cells, Case 4*

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
5	110	7.2	2.7	45.3	1.49
20	97	8.40	1.7	94	0.91
38	128	7.74	2.7	49	1.39
46	121	7.12	3	39	1.7

diameter of 6.5 microns. The degree of spherocytosis varied from borderline normal to definitely spheroid. The volume-thickness index varied from 1.4 to 1.9 and Castle's index from 48 to 36. The only atypical feature was the presence of a leukemoid blood picture during the period of observation, with a moderate number of normoblasts, erythroblasts, myelocytes and myeloblasts. The diagnosis was familial hemolytic anemia with ectopic hemopoiesis resulting in a leukemoid blood picture.

COMMENT

The finding of considerable variation in the volume-thickness relationship of normal red cells, as expressed by Haden's or Castle's method, is by no means an exception to the usual biologic rule. Furthermore, such variation is probably an expression of functional changes in the corpuscles of an individual as well as a normal morphologic difference between individuals. It is also in complete harmony with the limits of normal established for cell volume and diameter.

Apparently this series of cases represents the first determination of the range of the indexes of Castle and Haden. A comparable variation in thickness of

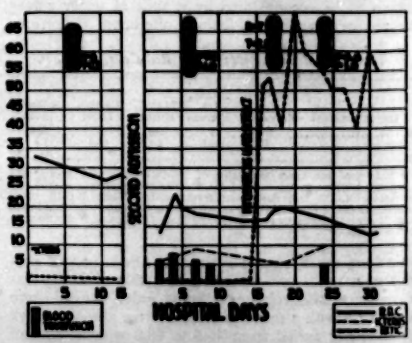

Chart 6.—Progress of the disease in case 6.

the red cells has already been reported by Price-Jones, Vaughan and Goddard, in which they found no correlation with the diameter. Unfortunately, no calculation of sphericity was made.

The interpretation of values for erythrocytic sphericity must be made with due regard to the normal limits as well as to possible physiologic variations in

the individual case. Many values previously reported as indicative of spherocytosis were undoubtedly within the normal range.

In the present series of cases the effect of physiologic changes probably accounted for a large measure of the variations seen. However, there was an undoubted general tendency to spherocytosis, since in every case but one there was at least one occasion when definite spherocytosis occurred. From this it is evident that only repeated examinations are of diagnostic significance unless values well beyond the normal range are obtained.

Decrease in the diameter of the erythrocytes appeared to be even more constant. In addition, a fairly definite relationship to spherocytosis was evident. As a rule, the thickest cells had the smallest diameters.

The one notable exception to microcytosis occurred in the fairly typical case 1. In this case a definitely macrocytic spherocytic corpuscle of enormous volume was seen in the first examination. The mechanism of production of this atypical variety of cell is not well understood. However, the explanation of Davidson

TABLE 5.—*Measurements of the Red Cells, Case 5*

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
2	86	6.8	2.4	48.6	1.4
12	81	7.3	2	68.3	1.65

TABLE 6.—*Measurements of the Red Cells, Case 6*

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
6 1st admission	71	6	2.5	40	1.64
6 2d admission	90	7.8	1.66	76.3	0.97
17	81	7	2.1	58.9	1.2
24	66	6.6	1.92	60.8	1.16

and Fullerton[18] is probably the most satisfactory, according to which megaloblastic transformation of the marrow is assumed as a result of hyper-regeneration. A rather prolonged hemolytic crisis of relatively severe degree, as seen in case 1, is apparently the stimulus to this type of response.

Another complicating factor must be considered in the diagnosis in rare atypical cases, namely coincident pathologic processes which tend to result in the formation of abnormally thin or abnormally large red cells. For example, cirrhosis of the liver exhibits both of these tendencies. Cases 5 and 6 evidently represent slightly different degrees of this type of complication. When studied together, the cases of these two brothers present conclusive evidence of two conditions tending to produce anemia but mutually opposed in their effect on corpuscular size and shape. In case 5 postmortem examination showed cirrhosis of the liver, while in case 6 the effect of liver therapy was definitely indicative of a similar mechanism. In addition, the unmasking of microcytosis corroborates the diagnosis of familial hemolytic anemia.

Finally, this study fails to reveal any correlation between the degree of spherocytosis and the severity of the disease. Neither was a definite relationship established between spheroid form and the onset of crisis, the rapidity of regeneration of the red cells or even the effect of splenectomy.

18. Davidson, L. S. P., and Fullerton, H. W.: Some Rare Types of Macrocytic Anemia, Quart. J. Med. 7:43-84 (Jan.) 1938.

SUMMARY AND CONCLUSIONS

Microcytosis was found on at least one occasion in six of seven cases of familial hemolytic anemia, while spherocytosis was found in five cases.

Spherocytosis may be absent in the presence of complicating factors such as cirrhosis of the liver.

Macrospherocytosis was observed in one case during crisis.

No significant correlation could be established between spherocytosis and the severity of the disease, onset of crisis, rapidity of regeneration of the red cells or effect of splenectomy.

ABSTRACT OF DISCUSSION

DR. RUSSELL L. HADEN, Cleveland: Dr. Hill has verified the observation that the increased tendency to hemolysis of red cells in congenital hemolytic jaundice is dependent on the spherocytic shape of the cell. I have recently studied a patient, however, who had the typical clinical picture of congenital hemolytic jaundice and spherocytosis of the red cells without increased fragility. I cannot explain this observation. Several factors influence the shape of the cell in congenital hemolytic jaundice. The simultaneous occurrence of an iron deficiency will flatten the spherocyte. If a deficiency in the erythrocyte-maturing factor supplied by liver occurs, the cell becomes larger. If a patient has anemia with cells of very small diameter, the disease is usually congenital hemolytic icterus and should be treated by splenectomy. On the other hand, hemolytic anemia with cells of large diameter should seldom be treated surgically. Dameshek has shown recently that under certain conditions, such as infection, the shape of the cell may change so that at times it is sufficiently spherocytic to be more fragile than normal. Thus the spherocytosis does not depend on heredity alone.

DR. M. C. RIDDLE, Portland, Ore.: Dr. Hill's paper points out that one cannot be too complacent in one's fixed ideas on the hemologic pictures of the various disorders discussed. It is extremely important that the clinical features of these diseases should be taken into account as well as the laboratory features. I have under observation a patient with familial jaundice which illustrates the features discussed. This patient has passed through three phases so far as the hemologic picture is concerned. In the first phase the typical hemologic picture of familial jaundice was present. Then there developed a leukemoid picture with a white count in the vicinity of 40,000, with considerable numbers of immature myeloid cells. In the third phase leukopenia and pronounced macrocytosis developed. The blood film was indistinguishable from that of pernicious anemia. This macrocytosis responded to the use of liver extract. I accounted for this response in much the manner in which Dr. Haden accounted for the macrocytosis discussed by Dr. Hill.

DR. JOSEPH M. HILL, Dallas, Texas: The time available did not permit a discussion of fragility. It is well known that undoubted hemolytic anemia may not be accompanied by increased fragility. This can be explained by the absence of spherocytosis at least during certain phases. I did find a rather definite relation between spherocytosis and fragility; in fact, it was more definite than the relation of clinical features and spheroid red cells. I believe that the use of liver therapy for this type of anemia is rational, since depletion of the stored erythrocyte-maturing factor apparently can result from prolonged excessive demand incident to increased erythropoiesis. This situation is apt to occur when the disease is unrecognized and untreated and there is damage to the liver. With regard to the leukemoid blood picture associated with this disease, there are probably two types: first, the acute crisis representing an outpouring of cells from the bone marrow and, second, the type that occurred in case 7. I believe that in this instance, with a compensated form of hemolytic jaundice, ectopic hemopoiesis resulted in lack of normal control of blood cell output. It may be difficult in such cases to differentiate the disease from myelogenous leukemia. The patient has been followed for five years, and I feel certain that he does not have leukemia, although at one time he was treated for it.

THE OUTLOOK IN THROMBO-ANGIITIS OBLITERANS

BAYARD T. HORTON, M.D.
ROCHESTER, MINN.

In the past decade I frequently have had anxious patients with thrombo-angiitis obliterans ask the question What is the outlook in my case? Hence the title of this paper. In an attempt to answer the question in such a manner that it may be of some service both to patients and to fellow workers in the field, I have carefully reviewed all the cases of thrombo-angiitis obliterans that have been observed at the Mayo Clinic from 1907 to 1937 inclusive. I have myself observed and studied a large number of these cases.

The past decade has witnessed marked changes in the attitude of physicians toward thrombo-angiitis obliterans largely because of a better understanding of the disease. Prior to this time the diagnosis of thrombo-angiitis obliterans carried with it the implication that amputation of one or both lower extremities would follow inevitably and, once the diagnosis had been established, it was suggested that amputation of the involved extremity be carried out promptly. For example Buerger,[1] in his book published in 1924, said that "amputation just above the middle of the leg" was performed in one case "because the little toe looked as though it was going to die off." At the clinic we have become more optimistic from year to year regarding the disease, and we feel that, if the diagnosis is made early and if the patient follows the thorough instructions which are given regarding the care of his extremities, he stands a good chance of continuing to walk on two feet throughout life.

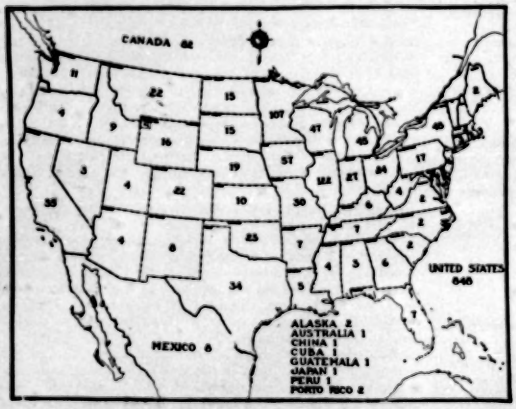

Fig. 1.—Geographic distribution of cases of thrombo-angiitis obliterans.

Thrombo-angiitis obliterans is a chronic occlusive arterial disease involving chiefly the extremities and affecting, for the most part, men between the ages of 20 and 50 years. In spite of the fact that it was formerly supposed to occur almost exclusively among Jews, it is now known to affect persons of all races. The cause of the disease has not been established. Its usual course is rather slow. As a rule the main vessels of the feet and legs are involved early, those in the upper extremities later.

The disease is characterized by a chronic relapsing lesion of the vessels in which the occlusive process and the development of collateral circulation struggle for supremacy. The element of time is most important in this struggle, since on it rests the preservation of the parts. If the intervals between relapses are short and the time for the development of collateral circulation is inadequate, trophic changes and gangrene are likely to ensue. Conversely, if the intervals between relapses are long, the collateral circulation becomes adequate and a sufficient supply of blood to the distal parts is assured. The first consideration regarding prognosis is therefore the frequency of exacerbations of the disease. Experience in a large number of cases shows clearly that the belief that amputation invariably will be necessary is not justified.

BASIS OF PRESENT STUDY

In the thirty-one years from 1907 to 1937 inclusive, 1,374 patients with thrombo-angiitis obliterans registered at the clinic. But since 426 of these patients registered more than once during this period, and some of them as many as ten times, the present study will be confined to the 948 individual patients represented (table 1). Throughout this report considerable material will be presented which bears on the old question of the relative susceptibility to this disease manifested by males and females and by Jews and Gentiles.

GEOGRAPHIC DISTRIBUTION

The patients in this series came from every state in the Union except Rhode Island, Vermont and New Hampshire; in addition there were patients from Canada, Mexico, Alaska, Australia, China, Cuba, Guatemala, Japan, Peru and Puerto Rico (fig. 1). They came from practically every walk of life. The same fundamental pathologic process was present in all cases and the signs and symptoms, as well as the clinical course, were strikingly similar. It is interesting to note that, while in the majority of cases of thrombo-angiitis obliterans the symptoms begin during the winter months, in this study the incidence of amputations in the warmer sections of the country, such as Florida and California, was as high as that observed in Minnesota and Canada (fig. 2). Therefore, in spite of the fact that patients went to live in warm sections of the country after having been observed at the clinic, amputations were still necessary. The explanation of this probably is that vasospasm in the collateral circulation does not disappear until the environmental temperature is 82 F. or above, as our studies at the clinic have proved. It is difficult to find in the United States a place where such a temperature is maintained.

AGE, SEX AND RACE

The distribution by age and sex is represented in table 2. The mean age of all patients was 41.8 years. More than 70 per cent of the 948 patients were in the

From the Division of Medicine, the Mayo Clinic.
Read before the Section on Practice of Medicine at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Buerger, quoted by Samuels, S. S.: The Diagnosis and Treatment of Diseases of the Peripheral Arteries, New York, Oxford University Press, 1936, p. 73.

third and fourth decades of life, the ages for the entire series varying from 17 to 73 years. The sex incidence is likewise of interest. Of the 948 patients twenty-one were women, which indicates an incidence of approximately 98 per cent in men.

I know of no other disease in which such common tissues as the veins and arteries are involved that is so exclusively confined to one sex as is thrombo-angiitis obliterans. No adequate explanation has yet been brought forth to account for this most unusual sex distribution. Too few cases of thrombo-angiitis obliterans have thus far been observed in women for one to compare adequately the severity of the disease as it affects them with its severity in the case of men. I have been under the impression that the disease runs a milder course in women than in men, but more cases will have to be observed for a longer period before conclusions in this respect can be drawn.

Of the twenty-one women patients, five were Jewish and sixteen were Gentiles. Of the 927 men, 257 were Jews and 670 were Gentiles. Thus roughly 28 per cent of the 948 patients were Jews and 72 per cent were Gentiles. In earlier reports [2] from the clinic, 55 per cent of the patients were Jews and 45 per cent were Gentiles. Thus far we have not observed thrombo-angiitis obliterans affecting a full-blooded Negro, although such cases have been observed elsewhere; one of our patients was, however, part Negro. More than twenty-eight different nationalities were represented in this series.

RACE AND DEGREE OF SMOKING

If a patient smoked five cigarets a day he was listed as a grade 1 smoker, if ten cigarets a day as a grade 2 smoker, if fifteen cigarets a day as a grade 3 smoker and if twenty cigarets or more a day as a grade 4 smoker (table 3). Many of the grade 4 smokers used as many as sixty cigarets a day. One patient, for example, smoked at least twenty cigarets before breakfast. Of the total of 948 patients who had thrombo-angiitis obliterans, 93 per cent were cigaret smokers; in 66 per cent of the cases the degree of smoking was graded 3 or 4.

Of the 262 Jews, 238 were smokers (table 3). Sixty-five of them were grade 1 or grade 2 smokers, and of these twenty-five, or 38 per cent, underwent amputation. Of the 173 grade 3 or grade 4 smokers fifty-eight, or 33 per cent, were subjected to amputation. Thus of the 238 Jewish patients who had thrombo-angiitis obliterans and who smoked, eighty-three, or 35 per cent, underwent amputation, whereas only 21 per cent of the nonsmokers were subjected to amputation. This report includes amputations elsewhere as well as at the clinic.

Of the 686 Gentile patients, 642 were smokers. Ninety of the 189 grade 1 or grade 2 smokers (48 per cent) were subjected to amputation; of the 453 grade 3 or grade 4 smokers 207 (46 per cent) underwent amputation. Of the forty-four Gentile patients who were nonsmokers sixteen, or 36.4 per cent, underwent amputation. Thus of all Gentiles who smoked 297, or 46 per cent, underwent amputation, whereas only 36.4 per cent of the nonsmokers were subjected to amputation.

It has been accepted generally that thrombo-angiitis obliterans is somewhat more severe among the Jews than among representatives of other races. This does not seem to be borne out by the present studies. Of the 262 Jews 33.6 per cent underwent amputation, whereas of the 686 Gentiles 45.6 per cent were subjected to amputation (table 3). These figures are for both sexes and for amputation performed both at the clinic and elsewhere.

The present study tends to indicate, however, that amputations were less frequent among nonsmokers. It has been difficult to persuade patients with thrombo-angiitis obliterans to stop smoking. In the past ten years numerous experimental studies have been reported in the American literature, which establish rather definitely that the use of tobacco does produce some vasospastic effects. Lampson,[3] Maddock and his co-workers,[4] Barker [5] at the Mayo Clinic, as well as Wright and Moffat [6] and Johnson,[7] have contributed important articles from this standpoint. Haggard and Greenberg [8] noted a definite elevation of the blood sugar following the use of tobacco. They were of the opinion that the mild hyperglycemic effect, as well as the effect on the blood pressure, might be a secondary result of the adrenal stimulation which is brought about by the action of nicotine on the sympathetic nerves and which results in an increased secretion of epinephrine. Herrell [9] recently has reported the case of a man, aged 57,

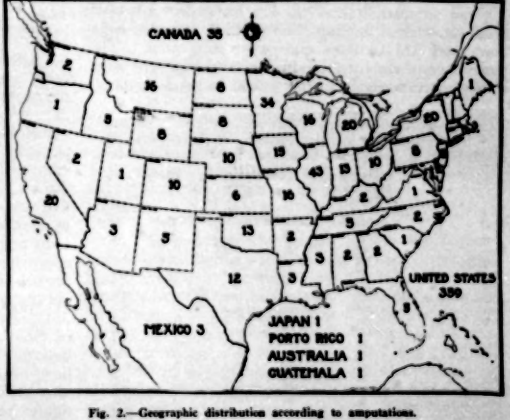

Fig. 2.—Geographic distribution according to amputations.

2. Brown, G. E.; Allen, E. V., and Mahorner, H. R.: Thrombo-Angiitis Obliterans: Clinical Physiologic and Pathologic Studies, Philadelphia, W. B. Saunders Company, 1928.

3. Lampson, R. S.: A Quantitative Study of the Vasoconstriction Induced by Smoking, J. A. M. A. 104: 1963-1966 (June 1) 1935.

4. Maddock, W. G.; Malcolm, R. L., and Colter, F. A.: Thrombo-Angiitis Obliterans and Tobacco: The Influence of Sex, Race and Skin Sensitivity to Tobacco on Cardiovascular Responses to Smoking, Am. Heart J. 12: 46-52 (July) 1936.

5. Barker, N. W.: Vasoconstrictor Effects of Tobacco Smoking, Proc. Staff Meet., Mayo Clin. 8: 284-287 (May 10) 1933.

6. Wright, I. S., and Moffat, Dean: The Effects of Tobacco on the Peripheral Vascular System; Further Studies, J. A. M. A. 100: 318-323 (Aug. 4) 1934.

7. Johnson, H. J., and Short, J. J.: Effect of Smoking on the Skin Temperature, J. Lab. & Clin. Med. 19: 962-966 (June) 1934.

8. Haggard, H. W., and Greenberg, L. A.: The Effects of Cigaret Smoking upon the Blood Sugar, Science 79: 165-166 (Feb. 16) 1934.

9. Herrell, W. E., and Cusick, P. L.: Vascular and Retinal Abnormalities Following Inhalation of Tobacco Smoke: Preliminary Report, Proc. Staff Meet., Mayo Clin. 11: 273-279 (May 4) 1936.

whose systolic and diastolic blood pressure invariably became markedly elevated and whose retinal arteries became constricted following the smoking of a cigaret.

AMPUTATIONS

It will be noted in table 1 and in figure 3 that according to the total registrations 15.6 per cent of the patients underwent amputation at the clinic. One hundred and seventy-eight of the patients were subjected to one or more amputations at the clinic, the total number of amputations performed being 214. Six of these patients were women, 172 were men. No amputations for thrombo-angiitis obliterans were carried out at the clinic from 1907 to 1916 inclusive, and the percentage of amputations from 1928 to 1937 inclusive was definitely less than during the previous ten years. Later in this report it will become evident from the statistics concerning amputation that progress has been made in the nonsurgical management of this disease.

Major and Minor Amputations.—In this study the loss of a finger or a toe was considered to constitute a minor amputation; the loss of a foot, a leg or a hand was considered a major amputation. Eighty-eight Jews and 313 Gentiles underwent amputation. The percentage of each of these two racial groups who were subjected respectively to major and to minor amputation is given in table 3. Of the total of 401 patients who underwent amputation 276, or 69 per cent, underwent major amputations; the remaining 31 per cent had minor amputations (table 3).

TABLE 1.—*Thrombo-Angiitis Obliterans (1907-1937 Inclusive): Distribution of Cases and Incidence of Amputations*

Year	Total Registrations of Patients with Thrombo-Angiitis Obliterans	New Cases		Amputations*	
		Number	Per Cent of Registrations	Number	Per Cent of Registrations
1937	73	39	53.4	5	6.8
1936	91	55	60.4	15	16.5
1935	98	61	62.2	22	22.5
1934	97	52	53.6	10	10.3
1933	101	57	56.4	15	14.8
1932	107	74	69.2	17	15.9
1931	109	64	59.2	16	14.8
1930	136	104	76.5	21	15.4
1929	113	91	80.5	7	6.2
1928	86	64	74.4	13	17.4
1927	62	49	79.0	14	22.6
1926	67	51	76.1	9	13.4
1925	47	39	83.0	8	17.0
1924	39	27	69.2	10	25.6
1923	33	30	87.9	4	12.1
1922	25	23	92.0	7	28.0
1921	22	18	81.8	7	31.8
1920	12	10	83.3	2	16.7
1919	16	13	81.2	4	25.0
1918	12	9	75.0	2	16.7
1917	12	10	83.3	2	16.7
1916	6	6	100.0	..	....
1915	5	4	80.0	..	....
1914	1	..	....	..	....
1913	1	..	....	..	....
1912	0	..	....	..	....
1911	1	..	....	..	....
1910	1	..	....	..	....
1909	1	1	100.0	..	....
1908	0	..	....	..	....
1907	1	1	100.0	1	100.0
Total	1,374	948	69.0	214	15.6

* At the clinic.

Seventy-one per cent of all amputations at the clinic for thrombo-angiitis obliterans from 1918 to 1927 inclusive were major amputations, whereas only 63 per cent of all amputations from 1928 to 1937 inclusive were major amputations. It is still more encouraging to note that during the past five years (1933-1937) only 48 per cent of amputations at the clinic were of the major type. This indicates definite progress in the medical and surgical management of this disease.

Amputations at Three, Five and Ten Year Periods After the Onset of the Disease.—In this phase of the study patients were divided into three, five and ten year groups, each group indicating the period of time which had elapsed since the onset of the condition. Thus of the 828 subjects in the three year group 694 (84 per cent) were followed for a period of three years from the onset of thrombo-angiitis obliterans. Of these 694, 215 (31 per cent) were subjected to amputation (table 4). This would indicate that approximately 70 per cent of patients who have thrombo-angiitis obliterans will go for three years after the onset of the disease without amputation being necessary. In the five year group 628 (80 per cent) of the 785 patients were traced and, of these, 248 (39.5 per cent) underwent amputations. This in turn would indicate that approximately 60 per cent of patients who have thrombo-angiitis obliterans will go for five years without the necessity of amputation. In the ten year group 334 (77 per cent) of the 433 patients were traced, and of these 39.9 per cent had amputations. This would indicate that approximately 40 per cent of patients who have thrombo-angiitis obliterans will go for ten years after the onset of the disease without amputation. These figures perhaps give a better insight into the outlook in thrombo-angiitis obliterans than anything else.

TABLE 2.—*Thrombo-Angiitis Obliterans (1907-1937 Inclusive): Age and Sex Distribution*

Age, Years	Males		Females		Total	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
10-19	2	0.2	..	....	2	0.2
20-29	84	9.1	4	19.0	88	9.3
30-39	302	32.6	7	33.3	309	32.6
40-49	375	40.4	9	42.9	384	40.5
50-59	146	16.0	..	....	146	15.6
60-69	14	1.5	1	4.8	15	1.6
70-79	2	0.2	..	...	2	0.2
Total	927	100.0	21	100.0	948	100.0
Mean age, years	41.8		38.8		41.8	
Per cent	97.8		2.2		100.0	

Bilateral Major Amputations.—Of the 948 patients, eighty-five underwent bilateral amputation of the legs; sixteen of these patients were Jews and sixty-nine were Gentiles. Eleven bilateral amputations were carried out at the clinic, all of the patients being Gentiles. Thirty-five per cent of these eighty-five patients who underwent bilateral amputations live in warm climates. Eighteen of the eighty-five are dead. At the clinic we have never had to amputate a hand because of thrombo-angiitis obliterans, but in this series of cases the hand of one subject had been amputated prior to his admission to the clinic; the hand of a second patient and both hands as well as both legs of a third patient were amputated after the patients left the clinic.

PHYSICIANS WITH THROMBO-ANGIITIS OBLITERANS

Twenty-two of the 948 patients were physicians, fifteen being Gentiles and seven Jews. Two of these twenty-two physicians underwent amputation, each losing a leg, and one of them later underwent lumbar sympathetic ganglionectomy at the clinic. Three of the twenty-two underwent bilateral sympathetic ganglionectomy at the clinic; not one of these has been subjected

to a major amputation since. One patient who had gangrene of the toes at the time of sympathectomy has since had the toes removed. Four of these twenty-two physicians are dead, one dying of cancer; the cause of death in the other three cases was not stated.

COMPLICATIONS

Thrombo-Angiitis Obliterans and Hypertension.—Of the 948 patients who had thrombo-angiitis obliterans 147 (15.5 per cent) had hypertension. Forty-three of the 147 are dead and twenty-two of the 147 underwent amputation.

Thrombo-Angiitis Obliterans and Diabetes.—Ten of the patients with thrombo-angiitis obliterans also had diabetes, the diabetes being relatively mild in nine cases. Six of the ten patients were Jews. All ten patients used tobacco averaging from fifteen to forty cigarets a day.

TABLE 3.—*Thrombo-Angiitis Obliterans (1907-1937 Inclusive): Amputations at Clinic and Elsewhere*

		Amputations					
		None		At Clinic		Elsewhere	
By race	Total	No.	%	No.	%	No.	%
Jews	262	174	66.4	33	12.6	55	21.0
Gentiles	686	373	54.4	145	21.1	168	24.5
Total	948	547	57.7	178	18.8	223	23.5

According to race and degree of smoking

	Total			Jews			Gentiles		
	Patients	Amputations No.	%	Total	Amputations No.	%	Total	Amputations No.	%
Nonsmokers	66	21	30.9	24	5	20.8	44	16	36.4
Smokers									
Grade 1	75	35	46.7	13	8	61.5	62	27	43.5
Grade 2	172	80	46.5	52	17	32.7	127	63	49.6
Grade 3	161	68	42.2	50	20	40.0	111	48	43.2
Grade 4	465	197	42.4	123	36	30.9	342	159	46.5
Total	948	401	42.3	262	86	33.6	686	313	45.6

Major and minor amputations by race and sex

		Major		Minor	
		No.	%	No.	%
Females	Jews	1	100.0		
	Gentiles	1	14.3	6	85.7
Males	Jews	62	71.3	25	28.7
	Gentiles	212	69.3	94	30.7
Total	Jews	63	71.6	25	28.4
	Gentiles	213	68.0	100	32.0

One of the Jewish patients had a toe amputated, one of the Gentiles a leg. One of the ten died a morphine addict.

The incidence of amputation in this small group was not any greater than in the group of patients who did not have diabetes. The part diabetes mellitus plays in the presence of thrombo-angiitis obliterans is not definitely known, but the indications are that if the diabetes is not adequately controlled it may tend to aggravate the course of the thrombo-angiitis obliterans.

SYMPATHECTOMY IN THROMBO-ANGIITIS OBLITERANS

One hundred and ninety-three of the 948 patients underwent either cervicothoracic or lumbar sympathetic ganglionectomy. Twenty-eight of the patients were Jews, 165 Gentiles. Ten of the Jewish patients later underwent amputation (eight major and two minor) and forty of the Gentile patients later underwent amputation (twenty major and twenty minor). Of the total 193 patients in this group, therefore, fifty (26 per cent) were later subjected to amputation. Five of twenty-one women patients underwent bilateral lumbar sympathetic ganglionectomy and one of the five also underwent cervicothoracic sympathetic ganglionectomy. Eight of these twenty-one women had amputations. Four of them were nonsmokers (two major amputations, two minor amputations); the other four were smokers and all underwent minor amputation.

It is well recognized that sympathectomy does not cure thrombo-angiitis obliterans. Probably it does not even alter the course of the disease in the blood vessels. It does, however, bring about the maximal blood flow to the sympathectomized extremities and for that reason is still the most logical surgical procedure in properly selected cases for increasing the blood supply.

TABLE 4.—*Thrombo-Angiitis Obliterans (1907-1937 Inclusive)*

	Amputations at Various Periods After Onset of the Condition											
	Three Years			Five Years			Ten Years					
Age, Years	Total Patients	Number Treated	Amputations Number	Amputations Per Cent of Those Treated	Total Patients	Number Treated	Amputations Number	Amputations Per Cent of Those Treated	Total Patients	Number Treated	Amputations Number	Amputations Per Cent of Those Treated
10-19	1	1	0	0	1	1	0	0	0	0	0	0
20-29	74	69	23	33.3	75	69	23	33.4	0	0	0	0
30-39	272	230	68	29.6	281	270	82	30.0	156	121	75	62.0
40-49	321	265	82	31.0	324	243	86	35.5	168	118	74	62.7
50-59	140	117	36	32.5	139	109	35	35.0	71	56	21	38.2
60-69	13	9	7	77.8	13	9	7	77.8	5	4	2	50.0
70-79	2	2	0	0	2	1	0	0	2	0	0	0
Total	823	694	215	31.0	785	628	248	39.5	433	334	209	59.9

CAUSES OF DEATH

One hundred and seventy-five of the 948 patients with thrombo-angiitis obliterans are known to be dead. Five of these were women. It is interesting to note that coronary heart disease ranked first as the cause of death, forty-seven (27 per cent) of the 175 patients having died of it. An additional twelve patients died of cerebral hemorrhage. Twelve patients died with gangrene or following amputation for gangrene, and seven died of fatal pulmonary embolism. The others died of known but unrelated causes.

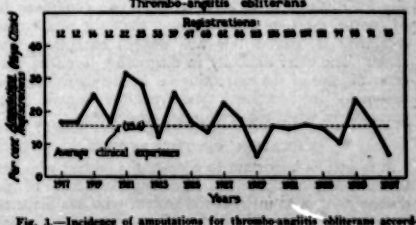

Fig. 3.—Incidence of amputations for thrombo-angiitis obliterans according to registrations.

PROGNOSIS

While in this study I have been able to tabulate many facts regarding this series of cases of thrombo-angiitis, no one could ever tabulate the loss of time and money, the pain and suffering and the tragedy of the loss of limbs incurred by these unfortunate persons. When one contemplates the large number of those who underwent major amputation, frequently of both legs and

occasionally of both arms, and who yet were able to carry on with a smile, one cannot help but think of Tennyson's lines "That men may rise on stepping-stones of their dead selves to higher things."

What, then, are the important factors which determine whether a person with thrombo-angiitis obliterans will live out his life expectancy walking on two feet, or whether he will fall into the unfortunate group whose extremities will have to be amputated? I believe that early diagnosis and thorough education of the patient concerning the nature of his disease and the care of his extremities will accomplish more in this respect than all other factors at the physician's command. Early diagnosis is important in order that the individual can avoid unnecessary delay in carrying out prophylactic measures to prevent the occurrence of gangrene. When it is recalled that at least 20 per cent of the patients who have come to the clinic with gangrene have had incisions made or nails removed for supposed infections of the digits, it becomes apparent that a working knowledge of the early signs and symptoms of thrombo-angiitis obliterans still is not widespread among members of the medical profession. The most frequent errors in diagnosis consist in mistaking claudication in the foot for evidence of arthritis or fallen arches and the abnormal rubor of the toes for evidence of infection. Pain in the arch of the foot on exercise suggests a structural defect in the bony support; hence most patients with thrombo-angiitis obliterans have had three or four pairs of arch supporters. Fortunately this error is much less evident now than it was ten years ago.

The essential point to establish, in the presence of symptoms referable to the hands, feet or legs, is whether the complaint is attributable to disease of the vessels and, if it is, whether the process is occlusive or vasomotor. The distinction between occlusive arterial disease and vasomotor disturbances can be made with accuracy in 95 per cent of cases by determining by simple palpation the presence or absence of pulsations in the four palpable arteries of the leg or in the two palpable arteries of the wrist. If the arteries are occluded there is more than a 90 per cent chance that the condition is thrombo-angiitis obliterans or arteriosclerosis obliterans. In the fifth decade of life the necessity for distinguishing between these two conditions is, of course, more or less academic, since the problem of treatment is, with a few well defined exceptions, the same. The chief difficulty in diagnosing localized vascular disease of the extremities is in distinguishing the vasomotor or functional type from the organic type, particularly when the lesions are associated.

EDUCATION OF THE PATIENT

It is just as important to educate the patient who has thrombo-angiitis obliterans regarding the nature of his disease as it is to instruct the patient who has diabetes mellitus regarding his diet. This cannot be accomplished in a few hours or even in a few days. Patients must be cautioned to avoid trauma and undue exposure to cold. Patients should also be taught to avoid crushing or bruising the feet or toes, and they should be instructed in the proper care of scratches, cuts, cracks, blisters and burns. The slightest abrasion should be carefully treated and regarded as if it were a major injury. New shoes should be worn for only a half hour to an hour the first day, and considerable time should be spent in breaking in such shoes. Soft woolen stockings should always be worn in cold weather. On many occasions simple abrasions produced by the wearing of new shoes have resulted in the formation of ulcers and in gangrene and amputation. Care of the toe nails is extremely important; it becomes more and more important as the blood supply to the digits decreases. Toe nails should be cut straight across, after being soaked in warm water, and they should be scrupulously but carefully cleaned. Corns, calluses and bunions should not be cut. Removal of ingrown toenails and minor operations on the toes in many cases have produced gangrene which in time has been followed by amputation. Such minor surgical procedures should be avoided except in rare instances and should then be performed only by a surgeon who is familiar with the problems involved in occlusive arterial disease.

Because of the poor blood supply to the feet, patients who have occlusive arterial disease may sustain injuries more readily than normal persons. They are also more susceptible to ill effects from exposure to cold. From the standpoint of cleanliness, the feet should be washed carefully and dried gently with a soft towel. Extreme care should be used in drying the skin between the toes. Brisk rubbing with a rough towel in many instances has produced ulcers. The occasional application to the feet and toes of a 50 per cent solution of alcohol is desirable, but this should not be used to excess. If the feet are excessively dry, or if the skin tends to crack or undergo scaling, hydrous wool fat or theobroma oil can be rubbed in gently to soften the skin. In numerous cases gangrene has been caused by the use of strong disinfectants, chemical compounds, ointments, corn cures and remedies for athlete's foot. It is unwise to use iodine, saponated solution of cresol, carbolated petrolatum or similar preparations as local disinfectants. Athlete's foot, which is a form of ringworm or trichophytosis, is frequently present in cases of thrombo-angiitis obliterans or arteriosclerosis obliterans and is usually worse in warm weather. This condition should receive appropriate care when it develops, as it is frequently the starting point of ulceration and gangrene between the toes. A safe method for treating athlete's foot is to soak the feet for a half hour each day in a 1:8,000 solution of potassium permanganate. This solution should be made up fresh for each soaking.

In spite of all the care which a patient may take, however, injuries to the toes and feet occasionally occur. When such a lesion develops, absolute rest in bed is indicated. In many a case in which gangrene has developed and the patient has lost an extremity he could perhaps have avoided such a calamity if he had taken the proper precautions early.

Smoking.—Mark Twain is reputed to have remarked that to stop smoking was the easiest thing he ever did, and he said he ought to know for he had done it a thousand times. Most patients who have thrombo-angiitis obliterans have had the same good intentions but have continued to smoke. Of the 948 patients, so far as I can determine only 106 stopped smoking. Eleven of these 106 expressed the opinion that the use of tobacco had been harmful to them. This phase of the problem is still being investigated.

About 50 per cent of those who stopped for varying periods resumed the habit, feeling that their symptoms were not improved after they had stopped. A rather large number, on the other hand, were convinced that smoking was the cause of their disease and said that they were greatly benefited after they stopped smoking.

Most of these gained weight, often from 15 to 20 pounds (7 to 9 Kg.) or more after they stopped smoking.

We at the clinic are of the firm conviction that all patients who have thrombo-angiitis obliterans should stop smoking. This, of course, brings up an interesting point as to the effects of tobacco on prognosis. A number of investigations have held that tobacco is the primary etiologic agent in the production of this disease, and yet, in this series, sixty-eight of the 948 patients had never used tobacco. Obviously the use of tobacco cannot be the cause of the disease, but it is evident, in the majority of cases, that excessive smoking does make the symptoms worse, although there are numerous exceptions even to this rule.

SUMMARY AND CONCLUSIONS

A total of 948 patients who had thrombo-angiitis obliterans were observed at the clinic from 1907 to 1937 inclusive. These patients came from every state in the Union except three and from ten foreign countries. More than twenty-eight different nationalities were represented. Two hundred and sixty-two (28 per cent) of the patients were Jews; 686 were Gentiles. The same fundamental pathologic process was present in all cases, and the signs and symptoms, as well as the clinical course of the disease, were strikingly similar. Twenty-one of the patients were women, the remaining 927 men; in other words, approximately 98 per cent of the patients were men. The mean age of the men was 41.8 years, of the women 38.8 years.

Of the 948 patients in the series 880 (93 per cent) were cigaret smokers. Of the 262 Jewish patients eighty-eight (33.6 per cent) underwent amputation, and of the 686 Gentile patients 313 (45.6 per cent) underwent amputation. Thus, 401 of the 948 patients underwent amputation either at the clinic or elsewhere. Eighty-five patients underwent bilateral amputation of the legs; sixteen of these patients were Jews and the remaining sixty-nine were Gentiles.

A study of amputations for three, five and ten year periods after the onset of the disease (table 4) indicates that approximately 70 per cent of patients will go for a period of three years from the onset without the necessity of amputation, whereas only 60 per cent will go for a period of five years and only 40 per cent for a period of ten years without being obliged to undergo amputation.

Perhaps the most important factors which determine whether a person who has thrombo-angiitis obliterans will continue to walk on two feet throughout life are early diagnosis and thorough education of the patient concerning the nature of his disease and the care of his extremities.

ABSTRACT OF DISCUSSION

DR. F. E. BOLLAERT, East Moline, Ill.: May I inquire about the recent treatment by suction pressure as well as the hyperemia treatment of these cases?

DR. BAYARD T. HORTON, Rochester, Minn.: The alternate suction and pressure apparatus is being used rather widely and we have used it for a number of years. I do not believe that we get any better results from the use of this machine than we can get from other simpler methods. I prefer the use of the Saunders bed to this alternate suction and pressure apparatus. With the use of the Saunders bed the patient must be kept in an environmental temperature of 82 degrees or above because one cannot get rid of vasospasm, particularly in the feet, unless the environmental temperature is at or above that level.

THE SURGICAL PATHOLOGY OF NASAL SINUSITIS

HERMAN SEMENOV, M.D.
LOS ANGELES

The first essential in the treatment of nasal sinusitis is an exact differential diagnosis of the surgical and nonsurgical types of disease condition present in the lining membranes. A lack of precise histopathologic knowledge in the past has led to the indiscriminate removal of tissues essential to the physiology of the nose and accessory sinuses. As every one knows, this has been attended by a striking array of contradictory results.

The purpose of this report is to recount in as much detail as possible the known types of sinusitis, the effects of allergy on the course of the sinus disease, the separation of reversible inflammatory from irreversible degenerative changes, and the character of the lining that forms after radical operations. The chief desideratum is a working principle which will delineate the types of disease present in every case and indicate the most appropriate treatment for each. The method of choice, selected from the several methods of treatment at hand, should completely remove the underlying disorder and most nearly conserve the normal functions of the nose and accessory sinuses.

MATERIAL AND METHODS

In this undertaking the histology and physiology of the sinuses were carefully reviewed and numerous normal membranes were taken from cadavers for measurement with the micrometer. The surgical specimens were measured at the principal point of disease and the results arbitrarily correlated with the exudative, proliferative and degenerative changes noted microscopically.

The material for the present report embraces more than a thousand sections collected and examined during the past ten years. The membranes were removed in one piece by careful subperiosteal dissection (Caldwell-Luc, transantral and external frontal ethmosphenoidal operations), mounted on cardboard supports or stretched over wads of cotton and fixed in 10 per cent solution of formaldehyde (fig. 1). They were sectioned by the paraffin method, stained as a routine with hematoxylin and eosin, occasionally with other methods of special staining, and in numerous instances with the Gram bacterial stain. The bacteriology of 400 sinuses was investigated by making swabs at the time of operation. Tissue cultures were made from 120 sinuses by grinding the membranes in sterile sand.

INCIDENCE OF ALLERGY IN SURGICAL CASES

1. *Nonallergic Cases* (47.6 per cent).—These include cases with a negative history of hay fever or asthma, absence of characteristic rhinologic signs (vasomotor rhinitis, bluish appearance of the turbinates) and lack of eosinophilia in the histologic preparations.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the author's reprints.

Read before the Section on Laryngology, Otology and Rhinology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

This work was started in 1928 under the facilities of the Noble Wiley Jones Fellowship in Pathology in the Department of Pathology of the University of Oregon Medical School in collaboration with Dr. Frank B. Kistner.

2. *Manifest Allergic Cases* (17 per cent).—These include cases with history, symptoms or signs of hay fever or asthma, suggestive bluish appearance of the turbinates, polypoid degeneration of the nasal mucosa and microscopic appearance of tissue eosinophilia, edema of the submucosa, hyaline degeneration of the basement membrane and mucoid degeneration of the overlying epithelium.

3. *Equivocal Allergic Cases* (35.4 per cent).—This group includes a large number of latent allergic conditions and a more or less variable number of pseudoallergic specimens in which the history was uncertain, vague or incomplete but in which microscopic examination showed tissue eosinophilia in association with one or more other histopathologic signs sufficient to warrant a presumptive diagnosis of latent allergy, if one were so inclined.

Nearly 52.4 per cent of the surgical cases presented histopathologic signs which suggested the possibility of an underlying allergy. Of this number at least 17 per cent were definitely allergic. More than 70 per cent of the obviously allergic cases presented superimposed suppurating infection.

Purulent sinusitis with exudate in the nose, diagnostic puncture (cytologic examination) and histologic sections was present in 72 per cent of all the cases. Nonpurulent sinusitis (hyperplastic, polypoid and cystic) was present in the remaining 28 per cent.

Nonpurulent hyperplastic, polypoid and cystic degeneration of the sinuses may arise as a consequence of either a suppurative process which has subsided or a nonsuppurative allergic process. Abscesses formed in 10 per cent and cysts in 33 per cent of the hyperplastic sinus membranes (thickening 1 to 2 mm.). The incidence of cysts and abscesses (50 per cent) was even greater in the cases in which polypoid degeneration developed (thickening 3 to 10 mm. or more). Bacteria were demonstrated by culture of the fluid in nearly half of the serous cysts. Typical cases with reports of the bacteriology and pathologic histology of nonpurulent sinusitis and several interesting cases of latent sinus infection without clinical signs of suppuration have been described in previous publications.[2]

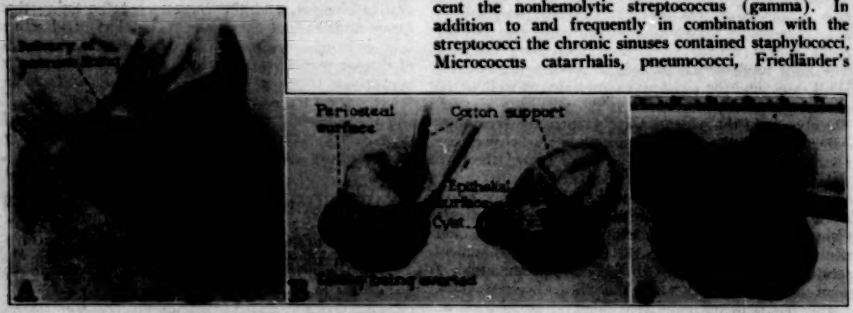

Fig. 1.—*A*, removal of specimen of sinus; *B*, method of mounting on cotton; *C*, specimen showing large serous mesothelial cyst.

Table 1.—*Chronic Sinusitis in Relation to Allergy*

Constitutional Background	Distribution of 500 Cases: Purulent Sinusitis, Cases	Purulent Sinusitis, Per Cent	Nonpurulent Sinusitis, Cases	Nonpurulent Sinusitis, Per Cent	Incidence of Allergy, Cases	Incidence of Allergy, Per Cent
Nonallergic	185	37	53	10.6	238*	47.6
Manifest allergic	60	12	25	5.0	85	17.0
Equivocal allergy	115	23	62	12.4	177	35.4
Surgical pathology	360	72	140	28.0	500	100.0

* Nonallergic.

bacilli, influenza bacilli, colon bacilli, diphtheroids and Streptothrix.

The virulence of the streptococci was tested in twenty rabbits and found to be pathogenic in seventeen. Various lesions were produced in the brain, heart, liver, kidneys, arteries and articular joints. Experimental arteritis and arteriosclerosis were produced in five rabbits with the hemolytic Streptococcus anginosus from a case of chronic sphenoiditis and large inguinal abscesses and myocardial and hepatic changes in two monkeys that were inoculated with the nonhemolytic Streptococcus mitis from a chronically infected antrum.[3]

A pure culture containing only one type of organism was found in only 20 per cent of the sinuses. Beta hemolytic streptococci appeared most frequently in purulent sinusitis. Staphylococci, especially the hemolytic type, also produced marked suppuration.

BACTERIOPATHOLOGY

Mixed infections of two or more organisms occurred in 80 per cent of the cases of chronic sinusitis. Streptococci predominated in both the swabs and the tissue cultures. They were present in 94.5 per cent of the cases. Staphylococci appeared in 70 per cent. Sixty-eight per cent of the chronic sinuses contained alpha and beta hemolytic streptococci, 14 per cent the nonhemolytic Streptococcus viridans (alpha), and 18 per cent the nonhemolytic streptococcus (gamma). In addition to and frequently in combination with the streptococci the chronic sinuses contained staphylococci, Micrococcus catarrhalis, pneumococci, Friedländer's

NORMAL HISTOLOGY OF THE MUCOPERIOSTEUM OF THE SINUSES

The sinus lining is less robust, less vascular and less glandular than the schneiderian membrane (fig. 2). Erectile tissue is lacking, the stroma is quite weak and rudimentary, and the entire lining is much thinner than the nasal mucous membrane.

2. Kistner, F. B.: Chronic Nonpurulent Sinusitis and Its Clinical Significance, Ann. Otol., Rhin. & Laryng. **38**:795 (Sept.) 1929; Histopathology and Bacteriology of Sinusitis, Arch. Otolaryng. **13**:225 (Feb.) 1931. Kistner and Semenov.[4]

3. Benson, R. L.; Smith, K. G., and Semenov, Herman: Experimental Arteritis and Arteriosclerosis Associated with Streptococcal Inoculations, Arch. Path. **12**:924, (Dec.) 1931.

The mucoperiosteum is composed of a single layer of pseudostratified ciliated columnar epithelium, which rests on a delicate basement membrane, and two layers of connective tissue: (1) a loose subepithelial areolar layer and (2) a compact periosteal layer (fig. 3*B*). Under normal conditions there are very few goblet cells in the epithelium and no signs of edema or round cell infiltration in the submucosa.

TABLE 2.—*Pure Cultures*

Bacteriology	Pathology	
	Purulent	Nonpurulent
Hemolytic streptococcus beta	18	1
Hemolytic streptococcus alpha	7	4
Nonhemolytic streptococcus viridans alpha	12	6
Nonhemolytic streptococcus gamma	14	3
Staphylococcus	11	5
	62 (70%)	19 (30%)
Total	81	

The normal sinus membrane is very thin, about 0.1 mm. in thickness, and may be compared to the membrana tympani, which is also 0.1 mm. in thickness.

The loose subepithelial layer has wide tissue spaces and usually becomes extremely edematous. The edema frequently ruptures the fibrils of areolar connective tissue and leads to the formation of mesothelial cysts. There is an astonishing degree of variation in the histologic structure of the subepithelial stroma. Some membranes are composed entirely of areolar tissue and these are prone to develop marked degenerative changes after trivial sinusitis; others are composed of a tougher periosteal type of stroma and successfully resist infection for many years (fig. 3).

The glands in the mucous membrane of the sinuses are relatively scarce. In the ethmoidal, sphenoidal and frontal sinuses submucous glands appear only in the neighborhood of the ostia.

In general the membrane of the maxillary sinus differs from that of the ethmoidal, the sphenoidal and the

Fig. 2.—Normal lining of ethmoidal sinus (*E*) compared with normal mucosa of middle turbinate attachment (*T*) and septum (*S*).

frontal only on its medial walls, where the structure is more complex owing to a rich supply of blood vessels and glands, which may be attributed to the earlier embryonic history of this part (paleosinus) in the development of pneumatization. The mucosa of the lateral wall of the antrum (neosinus) is poorly developed and resembles the frontal sinus in many respects. The lining of the antrum is loosely attached to the superior, posterior and lateral walls by delicate strands of connective tissue. The frontal membrane (pneumatization quite late in life) appears to be the most rudimentary of all the paranasal sinuses.

There are very few blood vessels in the mucosa of the sinuses and the circulation seems relatively poor.

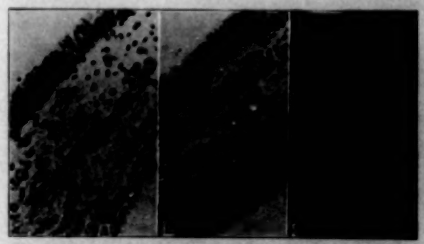

Fig. 3.—*A*, mucosa composed entirely of loose areolar tissue with rudimentary periosteum; *B*, normal mucoperiosteal arrangement; *C*, dense fibrous submucosa with very little loose tissue.

This may in part account for a slower rate of healing and a higher incidence of degenerative changes.

HISTOPATHOLOGY OF SINUSITIS

Increase in thickness of the membrane is caused partly by the cellular infiltration, partly by the edema of the connective tissue and partly by the proliferation of fibroblasts, which generally give the stroma a myxomatous appearance.

Cellular Exudation.—The leukocytic sequence in acute inflammation consists of an initial polymorphonuclear infiltration which is followed immediately by lymphocytes, eosinophils and mononuclear macrophages. All types of cells may be present in the subepithelial tissues within a period of fifty hours after the onset of the inflammatory reaction. The polymorphonuclear cells pass through the epithelium in great numbers and predominate in the pus that forms on the surface of the membranes. The lymphocytes and

TABLE 3.—*Thickness of Mucous Membranes of Sinuses*

	Normal Variations in Millimeters	Pathologic Thickening in Millimeters
Maxillary sinus		
Medial wall	0.3 - 1.0	1.0 -20.0
Lateral wall	0.1 - 0.5	1.0 -20.0
Frontal sinus	0.07- 0.3	1.0 - 4.0
Ethmoidal sinus	0.05- 0.4	1.0 - 5.0
Sphenoidal sinus	0.07- 0.5	1.0 - 5.0

plasma cells are inclined to remain within the tissues and for this reason predominate in the submucosal picture.

In 1927 Finck[5] noted the presence of eosinophilic infiltration in the nasal mucosa of allergic patients. In 1929 Kistner and I[6] confirmed this finding in the sinuses and with a few exceptions during the past ten years have found eosinophilic infiltration constantly present in allergic membranes. Numerous investiga-

5. Finck, H. P.: Tissue Changes in the Nasal Mucosa, Laryngoscope **37**: 783-797 (Nov.) 1927.
6. Kistner, F. B., and Semenov, Herman: Pathology of Sinusitis, Tr. Pacific Coast Oto-Ophthal. Soc., 1929; Ann. Otol., Rhin. & Laryng. **38**: 978 (Dec.) 1929.

tors, notably Hansel,[7] have studied the presence of eosinophils in smears of the nasal discharge and it is now a well established routine diagnostic method.

Mucoid Exudate.—The mucous membranes of the sinuses, as their name indicates, are moistened by a mucus-containing secretion. Under normal conditions only a small quantity of a limpid mucus is formed, but with the advent of irritation a more viscid secretion

Fig. 4.—*A*, goblet cells and mucoid degeneration in catarrhal sinusitis; *B*, hyperplastic ciliated epithelium in purulent sinusitis; *C*, epithelial metaplasia with leukocytic emigration.

appears. Most of the viscid mucus found in the sinuses is actually formed by mucoid degeneration of the surface epithelium.

Mucoid degeneration (fig. 4 *A*) is a very common process in the epithelium of the sinuses. It is manifest by the appearance of an abnormal number of goblet cells. The cilia are lost under these conditions and wide areas of sloughing epithelium, presenting only a remnant of basal cells, are frequently seen in allergic sinuses. This is one of the reasons why allergic sinuses are so frequently infected. In purulent sinusitis some areas show ciliated columnar cells, others hyperplasia (fig. 4 *B*), metaplasia (fig. 4 *C*) and focal necrosis (fig. 5). Hypertrophy and hyperplasia appear as defense reactions after chronic mucoid degeneration runs a protracted course.

Fig. 5.—Chronic purulent sinusitis with infection of the glands, edema, infiltration and necrosis of epithelium and cystic dilatation.

Proliferative Changes.—Hyperplasia is present when there is an increase in the number of cellular elements. Hyperplastic processes in all cases produce a tissue similar to that of the original part; hyperplasia of the epithelium gives rise to new epithelial cells, that of the glands to new gland cells, that of the connective tissue to new connective tissue cells, and so on. Hyperplasia of the stroma clearly follows acute inflammatory processes and bears the same relation to injury that the cicatrix and healing wound do to the granulation tissue from which they spring.

Proliferation of the connective tissue produces the greater part of the irreversible thickening of the sinus membranes (fig. 6). There is an increase in the number of fibroblasts and spindle and stellate cells. The subepithelial areolar layer tends to undergo polypoid degeneration (edema and a soft myxomatous tissue), but the more compact periosteal layer is more resistant to edema and infiltration. The periosteal portion tends to thicken and become more or less tough and fibrous during the course of chronic sinusitis.

The pathologic changes in hyperplastic sinusitis may be circumscribed or diffuse, involving either certain parts or the entire lining of the sinuses (figs. 6 to 9). The mild form of hyperplastic sinusitis tends to run a slow, insidious course with remissions and exacerbations. The exudative and edematous changes are

Table 4.—*Incidence of Degenerative Changes in Relation to Exudation and Thickening: 422 Cases*

	Purulent Sinusitis				Nonpurulent Sinusitis			
	Round Cells, Neutrophils		Round Cells, Neutrophils, Eosinophils		Lymphocytes, Plasma Cells		Lymphocytes, Plasma Cells, Eosinophils	
Type of Cellular Exudation	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Thickening, 1-2 mm.								
Cysts	3	5.3	1	1.9	6	20.0	13	27.5
Abscesses	3	5.3	1	1.9	3	10.0	4	8.5
Degeneration (irreversible)	6	10.6	2	3.8	9	30.0	17	36.0
Hyperplasia (edematous)	50	89.4	50	96.2	21	70.0	30	64.0
Totals	56		52		30		47	
Thickening, 2-5 mm.								
Cysts	16	19.0	38	38.0	11	50.0	15	47.0
Abscesses	6	7.0	13	13.0	0		0	
Degeneration (irreversible)	22	26.0	51	51.0	11	50.0	15	47.0
Hyperplasia (polypoid edematous)	61	74.0	49	49.0	11	50.0	17	53.0
Totals	83		100		22		32	

reversible and may subside completely after the exciting causes (allergy or infection) are removed, or they may continue on for weeks, months or even years without giving rise to symptoms. In the latent form of hyperplastic sinusitis, washings from the antrum usually contain numerous degenerating epithelial cells on cytologic examination.

DEGENERATIVE CHANGES

1. *Retention Cysts.*—Obstruction of the gland ducts by leukocytic infiltration (fig. 5) initiates the formation of retention cysts, and as each acinus becomes cystic it encroaches on the adjacent glands; eventually the dilated tubules rupture into one another. The interior of a retention cyst is lined with epithelium in various stages of degeneration. Sometimes there are areas devoid of epithelium bordering on areas of flattened cells which gradually pass over into columnar cells, and finally one may find mucous or goblet cells. It is probable that the epithelial variations represent stages in the cystic evolution. Retention cysts contain a thick mucoid material which sometimes is mixed with concentric deposits of epithelial débris and leukocytes.

7. Hansel, F. K.: Allergy of the Nose and Paranasal Sinuses, St. Louis, C. V. Mosby Company, 1936.

2. *Mesothelial Cysts.*—When the tissue spaces of the loose areolar stroma become extremely edematous, they frequently rupture and form large cystic cavities. These cysts have no epithelial lining. They are usually thin walled and in the absence of suppuration are filled with a clear amber fluid (fig. 1 *C*).

Cystic degeneration appeared in one third of all the cases of chronic sinusitis. It was greater in the mucous membranes that were more than 2 mm. in thickness (50 per cent), especially in the allergic specimens. Normal glands were found in only 15 per cent and cystic dilatation with abscess formation in 85 per cent of the manifest allergic cases. Abscesses appeared in from 5 to 15 per cent of the purulent sinuses.

3. *Polypoid Degeneration.*—Polypoid degeneration, whether it is bacterial, allergic, catarrhal or suppurative, is always characterized by great edema, which may be attributed to impaired circulation, abnormal capillary permeability and lymphatic obstruction in a delicate stroma. There are many other factors responsible for this condition, but the loose histologic structure of the mucosa of the sinuses and the presence of chronic edema (allergy or chronic infection) are the evident predisposing factors.

Polyps consist of a water-logged myxomatous connective tissue in both the nose and the paranasal sinuses. Eosinophilia was found in more than two thirds of the

Fig. 6.—A, normal thickness of lining; *B*, hyperplastic sphenoidal membrane, ten times normal thickness. Figures 6, 7, 8 and 9 are reduced from photomicrographs with a magnification of ten diameters.

polypoid specimens. These cases were considered allergic; no evidence of eosinophilia was found in one third of the cases and the pathologic condition was considered nonallergic.

In a recent publication Kern and Schenck [8] stated that allergy is a constant factor in the etiology of nasal polypi. They believe that nearly 100 per cent of mucous polyps are allergic in origin. Walsh and Lindsay [9] in a well controlled investigation of seventy-five cases of nasal polyposis found that some were associated with allergy and others with nonallergic infection of the nasal accessory sinuses. The nonallergic polypi are usually unilateral, and removal is followed by better results than removal of allergic polypi, which are frequently bilateral.

Polypoid degeneration throws the surface of the mucous membrane into crypts and pockets, which retain much infection and interfere with ciliary action. Nonallergic polypoid sinusitis demonstrating mesothelial cystic degeneration may be seen in figure 7. Allergic sinusitis with extensive formation of mucus and marked polypoid edema of the loose areolar tissue may be seen in figure 8. Marked polypoid degeneration with a large mucous cyst and a large mesothelial cyst may be seen in figure 9. This specimen is from a patient with allergy and demonstrates the great tendency of allergic sinusitis to develop into pronounced degenerative changes.

Choanal polyps sometimes form in the sinuses, especially in the antrum, and extrude through the ostium into the nasopharynx. The origin of these polyps is frequently on the lateral wall of the antrum (fig. 10). I have often wondered why this should be so; one would ordinarily expect polypi to begin near the ostium

Fig. 7.—Polypoid degeneration in chronic purulent sinusitis, nonallergic. Thickening from ten to forty times normal.

where the greatest amount of irritation and discharge is to be seen. The answer lies, I believe, in the histology and embryology of the antrum. The lateral portion, as has already been stated, is extremely thin, changes quite late in life and belongs to the rudimentary neosinus. It is therefore quite delicate and subject to greater degenerative changes, since the blood supply and lymphatic drainage of this region are so vulnerable.

According to André,[10] Grunwald [11] and Mullin and Ryder,[12] the lymphatic channels lie in the membranes and follow a circuitous course to the ostium. Obstructive processes, either vasomotor, allergic, infiltrative or inflammatory, have many opportunities to interfere with this extended line of communication and may easily give rise to back pressure, chronic hydrops mucosae and polypoid swelling on the lateral wall of the antrum.

Considerable absorption of bone and osteoporosis accompany polypoid degeneration. Every one is familiar with osteoporosis of the middle turbinate in polypoid degeneration of this structure. I have several times seen extreme absorption in the canine fossa as a result of the chronic hyperemia and stasis associated with polypoid degeneration within the antrum. A pyogenic

Fig. 8.—Polypoid allergic sinusitis from fifteen to fifty times normal thickness.

8. Kern, R. A., and Schenck, H. P.: Allergy a Constant Factor in the Etiology of the So-Called Mucous Nasal Polyp, J. Allergy **4**:485 (Sept.) 1933.

9. Walsh, T. E., and Lindsay, J. R.: Cytology of Nasal Polypi, Arch. Otolaryng. **20**:649 (Nov.) 1934.

10. André, J. M.: Contribution a l'étude des lymphatiques du nez et des fosses nasales, Thesis, Paris, 1905; Recherches sur les lymphatiques du nez et des fosses nasales, Ann. de mal. de l'oreille, du larynx., etc. **31**: 425, 1905.

11. Grunwald, L.: Die Lymphgefasse der Nebenhohlen der Nase, Arch. f. Laryng. u. Rhin. **23**:1, 1910.

12. Mullin, W. V., and Ryder, G. T.: Studies on the Lymph Drainage of the Accessory Nasal Sinuses, Laryngoscope **31**:158 (March) 1921.

process seldom creates this condition. As a matter of fact, pyogenic inflammation often leads to formation of new bone and fibrosis.

REGENERATION AND HEALING OF THE MUCOUS MEMBRANE OF THE SINUSES

There are few, if any, references in the available literature to the microscopic appearance of the mucous membranes of the sinuses after inflammation has subsided and complete healing has resulted. The question frequently arises Does sinusitis ever heal completely and what happens when it heals without operation? These questions may be answered by the following case:

A man aged 50 had apparently recovered without surgical treatment from a chronic mucopurulent sinusitis of twenty-five years' duration. For a period of four years he was free from colds, nasal discharge and sinal symptoms. X-ray examination of the sinuses revealed definite thickening and blurring of the antrums, ethmoids and sphenoids. The mucous membranes were removed, sectioned and found to be many times the normal thickness. When examined under the microscope, the epithelium was perfectly normal. The submucous connective tissue, instead of being loose and areolar, was thick and fibrous (fig. 3*C*).

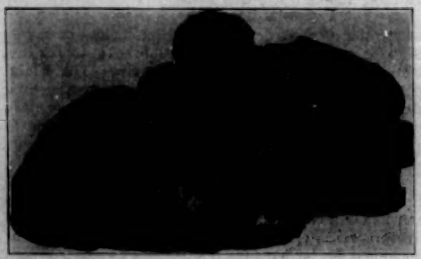

Fig. 9.—Polypoid and cystic degeneration in allergic sinusitis, showing mesothelial cyst and retention cyst. From fifty to seventy times the normal thickness.

The stroma was fully 2 mm. thick. There were no signs of edema, inflammation or degeneration. The glands were compact and surrounded by firm connective tissue.

This interesting mucoperiosteum apparently became tougher and stronger as the years went on. Similar changes have been noted in the ethmoidal, sphenoidal and maxillary membranes in several other cases. Healing by fibrosis is a desirable end result as far as the sinuses are concerned.

Postoperative Repair and Regeneration of Sinus Lining.—The blood clot on the denuded osseous wall gradually organizes and becomes converted into scar tissue. Epithelium spreads from the bordering nasal mucosa and gradually covers the surface of the scar tissue.

In previous publications Kistner and I [13] called attention to the presence of scar tissue and the variability of the epithelial regeneration, especially the cilia. This does not mean that the cilia are absent altogether, for we have always maintained that healing varies from place to place and from person to person and there is no reason why it should not produce perfectly normal epithelium in some cases. From a practical point of view, however, the postoperative membrane is a poor substitute for the original mucous membrane of the normal sinus. Hilding's [14] physiologic experiments in the frontal sinuses of dogs demonstrate the existence of impaired ciliary function in those areas in which the mucous membrane has been removed and permitted to regenerate. This postoperative condition of the lining, on the other hand, is much better than a pathologic sinus full of polypi, cysts and abscesses, but one should not justify radical surgery on the assumption that the postoperative condition of the tissue is normal sinus mucoperiosteum.

COMMENT

Anatomic obstructions, such as deflections of the nasal septum, concha bullosa and similar abnormalities, are predisposing factors in the etiology of chronic sinusitis. Repeated attacks of nasal congestion with thickening and polypoid degeneration are frequently due to an allergic constitution. Allergy is a predisposing factor in nearly half of the cases of sinusitis. Trauma, epidemic colds and bacterial invasion by extension from neighboring foci of infection such as dental abscesses, oro-antral fistulas and osteomyelitis of the jaw have long been known to be exciting factors.

The treatment of chronic sinusitis may terminate successfully after the offending obstructions and hypersensitiveness to extrinsic allergens have been corrected.

Exudative changes are frequently reversible when ventilation and drainage are established. Degenerative changes with pronounced thickening of the mucous membrane rarely respond to simple drainage and usually require radical surgery of the sinuses (fig. 10*B*). A subacute mucopurulent sinusitis often responds to the Proetz displacement method of irrigation and suction. A suppurative infection, however, with empyema of the sinuses may require surgical intervention before adequate drainage is obtained. Chronic purulent sinusitis that fails to respond to conservative methods of drainage invariably shows deep seated infection of the glands and cystic degeneration of the submucosa (fig. 5).

Nonpurulent hyperplastic sinusitis rarely requires surgical intervention. Nearly two thirds of the cases are due to allergy, especially when a bilateral process is present. The allergic constitution predisposes one to pansinusitis and degenerative changes of the mucous membrane of the entire upper respiratory tract. For this reason it is well to treat the underlying allergic condition before serious consideration is given to surgical intervention. Purulent sinusitis in an allergic individual should be treated simply as a local problem of drainage. The results, however, are not as brilliant as in nonallergic persons. Healing is more sluggish and polypoid edema tends to appear even in the granulation tissue. With this in mind I believe that the statistics of the future will show a higher incidence of cured sinusitis once the allergic conditions are recognized as such and treated with the same consideration that is afforded syphilitic and tuberculous conditions.

SUMMARY

1. The microscopic changes of the sinal mucoperiosteum in several hundred surgical specimens show that thickening in excess of 2 mm. is associated with deep seated degenerative changes in 50 per cent of the cases.

13. Semenov, Herman, and Kistner, F. R.: Repair in the Paranasal Sinuses of Man Following Removal of Mucous Membrane Lining, Proc. Soc. Exper. Biol. & Med. 27:322 (Jan.) 1930. Kistner, footnote 2, second reference.

14. Hilding, Anderson: Experimental Surgery of the Nose and Sinuses: II. Gross Results Following the Removal of the Interinous Septum and of Strips of Mucous Membrane from the Frontal Sinus of the Dog, Arch. Otolaryng. 17:321 (March) 1933.

2. Purulent sinusitis constitutes 72 per cent of the cases. Nonpurulent hyperplastic polypoid and cystic degeneration constitutes 28 per cent of the cases.

3. Degeneration of the mucous membrane of the sinuses may be explained in part by the rudimentary microscopic structure of the stroma. A preponderance of loose areolar tissue favors the formation of mesothelial cysts and polypoid degeneration. Membranes of the sinuses endowed with a more fibrous periosteal type of stroma are resistant to the same pathologic processes. The healing power in such a membrane is shown in the case described as it appeared after twenty-five years of mucopurulent sinusitis.

4. Manifest allergic sinusitis occurs in 17 per cent. Nonallergic inflammation of the sinuses as determined by a careful history and examination of the patient and histologic preparations appeared in 47.6 per cent of the cases.

5. The allergic membrane is prone to infection and resistant to treatment. Degenerative changes are greater in allergic sinuses. Hyperplastic sinusitis, especially the bilateral type, is allergic in 70 per cent of the nonpurulent cases.

Fig. 10.—*A*, polyps arising in the antrum attached to the lateral wall and projecting through the ostium into the nasal cavity; *B*, multiple cystic abscesses in right and left maxillary sinus from a patient with chronic purulent degenerative allergic sinusitis.

6. Tissue cultures reveal a preponderance of streptococci and staphylococci in chronic sinusitis, mixed infection being present in 80 per cent.

7. Exudative sinusitis usually responds to conservative treatment. Degenerative changes which are irreversible in character require radical treatment.

8. Postoperative healing in the paranasal cavities is accomplished by the formation of a dense layer of white fibrous connective tissue which epithelizes by an ingrowth of nasal mucosa.

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ABSTRACT OF DISCUSSION

Dr. Roy F. Nelson, Oakland, Calif.: Pathology is a basic science. I fear I am becoming hypersensitive to the word "allergy." I have a healthy skepticism, doubting whether it is really known what is meant by that word. I know that allergy exists clinically, usually caused by extrinsic foreign proteins and amenable to treatment. However, sometimes "allergy" is used too loosely and has little meaning except "different" or not otherwise understood. Dr. Semenov's classification of "equivocal allergy" is good, but might one not better find some other term altogether? I doubt that eosinophilia and polyposis are necessarily diagnostic of allergy in the accepted clinical sense. Fifty per cent of "equivocal allergic" manifestations in surgical cases is entirely too high. The incidence of frankly degenerative changes (abscesses, fibrosis, myxomatous degeneration and so on) is too high. I wonder whether this which we are supposed to accept as allergy might not better be called a characteristic reaction of some people to insult. If this insult is from foreign protein to which they are sensitive, one has manifest allergy. But this reaction may appear to infection or even to chemical insults, and the reason some individuals so react is as yet unknown. At any rate Dr. Semenov's facts show that the rhinologist should not in the presence of this "equivocal allergy" abandon the field. He should study his case more intensively, review the history and every factor involved with meticulous care, and frequently ask for the help of the allergist; but he should not abdicate and should realize that even complete and extensive surgical operation may be necessary in obtaining results. Pathologic classifications cannot be dogmatically applied to individual cases.

Dr. Raymond O. Dart, San Francisco: Dr. Semenov's comprehensive research into the anatomy of the paranasal sinuses is of practical value to the general pathologist. In the aggregate, it is probable that a greater number of rhinologic specimens are examined by general pathologists than by specialists in the field of rhinology. The general pathologist looks to the specialist for the researches which pave the way for him to make more accurate diagnoses in his routine work. In the available literature on the subject, little is found on the normal anatomy of the paranasal sinuses, and the classifications of the various pathologic processes found in these membranes are varied and confusing. The recognition of allergy as the basic pathologic condition in a large proportion of cases has added to the diagnostic difficulties of the general pathologist. It is not surprising, therefore, to find conflicting reports on the results of the treatment of these cases. Dr. Semenov has defined the limits of the normal anatomy of the paranasal membranes and outlined a workable classification of the various pathologic processes. It is interesting to note that in 35.4 per cent of the author's cases histopathologic conditions suggestive of allergy could not be correlated with clinical history or symptoms. This, together with conflicting reports of other investigators concerning the incidence of allergy and its relation to sinusitis, would indicate that there is need for further and more comprehensive work on this phase of the subject. It is suggested that further studies in this field might be undertaken in a cooperative effort by rhinologists by means of a registry of rhinologic pathology. The splendid results obtained from existing registries are well known. The purpose of most registries has been the study of cancer. Other diseases than cancer might well be made the subject of a comprehensive registry study. A start in this direction was made by the American Academy of Ophthalmology and Otolaryngology when it established the registry for the Section on Laryngology, Otology and Rhinology. Selected cases from this registry were used to prepare the loan sets of otolaryngic pathology now available to members of the academy who are preparing for the examinations of the board. An active registry study of the subject of sinusitis would undoubtedly result in greater understanding of the underlying pathologic principles with consequent improvement in diagnoses and methods of treatment.

The First State Hospital.—About 1830 a vigorous movement having for its object the erection of suitable state hospitals for the insane manifested itself simultaneously in several states. This movement found its first concrete expression in Massachusetts with the opening, in 1833, of the State Lunatic Hospital at Worcester.—Deutsch, Albert: The Mentally Ill in America, New York, Doubleday, Doran & Co., Inc., 1937.

Clinical Notes, Suggestions and New Instruments

EXTREME OBESITY FOLLOWED BY THERAPEUTIC REDUCTION OF TWO HUNDRED AND THIRTY-NINE POUNDS

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Associate Clinical Professor of Medicine, New York Post-Graduate Medical School of Columbia University

The question of how much or at what rate weight may be removed safely is a moot one. From 395½ pounds (180 Kg.), the patient whose case is reported here reached a low weight of 156½ pounds (71 Kg.) in twenty months, with progressive improvement in health throughout the period and subsequently.

REPORT OF CASE

L. G., a woman aged 32, Russian, a housewife, applied to the Obesity Clinic for weight reduction on March 22, 1935. She had always been overweight. At 17, when she was married, she weighed 260 pounds (118 Kg.). There had been no change in her mode of living. She considered that her optimum weight

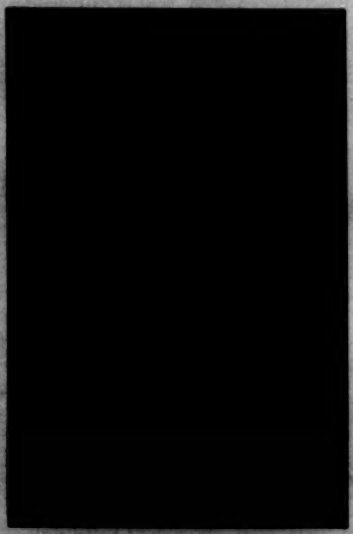

Fig. 1.—Patient when she weighed 402 pounds.

subjectively had been 195 pounds (88.5 Kg.); her maximum weight had been 402 pounds (182.3 Kg.). She slept from eight to ten hours a night, used little tobacco and no alcohol, and had a very good appetite. There were no gastrointestinal symptoms nor any relative to the extremities, such as varicose veins, fallen arches, painful knees or edema. The menses had been irregular since onset, with the exception of the three months just prior to admission, when they followed a twenty-eight day cycle, each period lasting about two and a half days. She had suffered from psoriasis since the age of 8 years.

Her father was of normal weight. Her mother weighed approximately 300 pounds (136 Kg.) and suffered from diabetes. Her brother had weighed 230 pounds (104 Kg.) maximum but at that time weighed 185 pounds (83.9 Kg.). One sister was obese at 185 pounds. There was no history of hypertension or of cerebral accidents. Two sisters and one brother had died in infancy.

Her height was 63 inches (160 cm.), weight 395½ pounds (the estimated normal was 145 pounds [65.8 Kg.]). The skin showed rather extensive psoriasis, the teeth showed evidence of mild pyorrhea and the tonsils were hypertrophied and cryptic. The arteries were not unduly thickened and the blood pressure was 160 systolic, 120 diastolic. There were a few moist rales at the base of the right lung. The size and contour of the heart were not determined and the abdominal organs were not palpated because of extreme obesity. The physical examination was otherwise essentially negative.

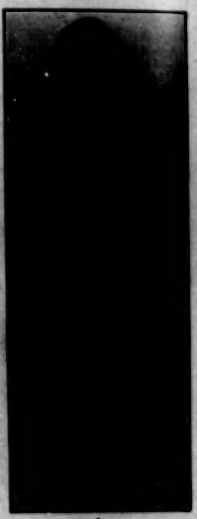

Fig. 2.—After course of treatment when the patient weighed 186½ pounds.

The urine was normal. Dextrose tolerance tests (done by giving the patient 100 Gm. of dextrose in the postabsorptive state) at the fasting and one and two hour periods were respectively 113, 160 and 154 mg. per hundred cubic centimeters of blood March 28, 1935, and 80, 125 and 125 mg. July 14, 1936. At the time of the second dextrose tolerance test, definite hypoglycemic symptoms had become manifest. The urine sugar was negative at all times. Basal metabolic rates are shown in table 1. Blood urea nitrogen was 13.5 mg. and nonprotein nitrogen 32 mg. per hundred cubic centimeters.

This was considered a case of simple obesity, the result of prolonged overnutrition. There were no manifestations to indicate an endocrine etiology.

For treatment she was given a diet, with occasional variations, of approximately 600 calories, which consisted of 35 Gm. of carbohydrate, 70 Gm. of protein and 20 Gm. of fat. Thyroid extract was given in a dose of 3 grains (0.2 Gm.) daily after the second basal metabolism test of April 9, 1936. This was varied from time to time according to indications. The patient followed orders faithfully throughout the entire period from March 22, 1935, to Nov. 17, 1936, at which time she weighed 156½ pounds without clothing. A record of her weight losses is shown in figure 4 and table 2.

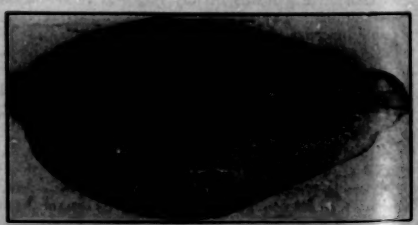

Fig. 3.—Excess skin removed by operation, measuring 24¼ by 12¼ inches.

September 29 she was referred to Dr. Gustave Aufricht of the department of surgery for the removal of excess skin and subcutaneous tissue. At that time her weight was 177½ pounds (80.5 Kg.). Over the abdomen there was a rather large apron

From the Medical Clinic of New York Post-Graduate Hospital.

of skin, which was removed by operation October 27 and weighed 5½ pounds (2.5 Kg.). She made a good recovery and was discharged November 17.

COMMENT

The patient's health remained excellent throughout the entire period of reduction. At no time did she complain of hunger or weakness. There was a moderate improvement in the psoriasis, and the skin showed remarkable adaptability to the smaller proportions. At a weight of 156½ pounds she was in excellent health and spirits, and there was little, when she was clothed, to indicate that she had ever been obese.

During the first months of the reduction period the patient's average loss was 12 pounds (5.4 Kg.) a month. In my experience most patients show an average loss of weight over prolonged periods of 10 pounds (4.5 Kg.) a month.

This case would indicate that there is no limit in the extent to which excess weight may be removed by submaintenance diets, provided such diets contain adequate protein, minerals and vitamins, together with moderate amounts of carbohydrate. Fats may be minimal. To insure sufficient vitamins, these are often added, as such, in concentrated form. Dairy products, such as skim milk and cottage cheese, are valuable in providing adequate calcium and phosphorus. Reductions of from 10 to 20 pounds a month over considerable periods have not been attended by any untoward symptoms in my experience. These observations are entirely in accordance with those of Evans and Strang,[1] who advocate rapid reduction of weight on low calory diets.

An important feature of this case was the high initial total heat production. This, since fat cells themselves are largely inert,[2] in persons who are overweight has the same significance as the "basal" metabolism in those of normal weight and is of far greater importance in indicating the energy exchange of the nonfatty energy-producing tissues of the body.

The figure used to indicate the total heat production is a percentage above or below that which would be produced if the individual were of normal weight (therefore of normal surface area) and had a normal rate of heat production. It is obtained by determining the ideal weight for the individual and from this and the height combined the normal surface area in square meters. This is then multiplied by the calories, per square meter per hour, that the person should have; i. e., the normal basal metabolism figure. The resultant figure represents the total calories per hour that the person should produce at ideal weight. A comparison with the actual caloric output per hour gives the percentage above or below the normal. This is identical with the current method of expressing the "basal" metabolism, which is also given as a percentage above or below an average normal.

No confusion need be experienced in understanding these two methods of expression if it is remembered that "basal" metabolism relates to heat production under standard conditions per unit of body surface and that total heat production relates to the body as a whole. This important distinction has been too generally ignored. Clinicians have often assumed in the study of overweight that, since the "basal" metabolism is reported normal, the patient's rate of metabolism is also normal. The opposite is actually the case, since the total energy output of the obese is almost invariably too high. The extent to which the metabolism rises depends on the degree of overweight and the consequent increase of surface area. The increase of total heat production, therefore, is in direct proportion to the increase in surface area, provided the "basal" rate remains constant.

In the case under discussion, the total heat production originally was 56 per cent above normal. This might well be compared to a case of normal weight with hyperthyroidism, in which the "basal" metabolism is +56 per cent. Many overweight patients exhibit symptoms similar to hyperthyroidism—hypertension, tachycardia, stimulation of the sympathetic nervous system and diminished dextrose tolerance. This, in my opinion and in that of other observers,[3] can be directly related to the increased metabolism.

The return of the total heat production to normal limits with restoration to ideal weight, as seen in this case, is characteristic. Coincidentally there was a marked subjective improvement throughout the reduction period and an improvement in the dextrose tolerance until symptoms of hypoglycemia were experienced.

To counteract the characteristic decline of the metabolic rate resulting from submaintenance diets (presumably due to a loss of the specific dynamic action of foodstuffs and possibly other factors) I employ thyroid extract in adequate dosage. This dosage has been controlled in a considerable number of cases by repeated determinations of the metabolic rate. Thyroid has been consistently used in the clinic to offset the falling rate of metabolism resulting from reducing diets and to maintain a satisfactory weight loss. Though not well tolerated early for the obvious reason of an increased metabolism, it is well tolerated later, after the effect of the reducing diet has manifested itself.

502 Park Avenue.

TABLE 1.—*Metabolism Studies*

Date	Height, Inches	Weight		Surface Area		Basal Metabolism		Total Heat Production	
		Pounds	% Above Normal	Square Meters	% Above Normal	Calories per Sq. M./Hr.	% Above Normal	Calories per Hour	% Above Normal
4/ 1/35	62.6	297	173.8	2.56	58.3	36.79	+ 1.6	94.07	+56
4/ 9/36	63.0	229½	50.8	2.03	20.8	32.57	−10.8	65.51	+ 7
11/17/36	63.2	156½	8.9	1.72	2.4	32.54	−10.1	55.97	− 7

TABLE 2.—*Reduction Record of Patient*

Date	Weight, Pounds	Blood Pressure	Comment
3/22/35	285½	.....	Diet: calories 600; carbohydrate 25, protein 70, fat 20
5/31/35	257½	134/112	
8/25/35	213½	120/ 80	
10/25/35	202½	.....	
12/27/35	200	122/ 90	Menses regular
3/13/36	227	116/ 94	Feels well
5/27/36	204	128/ 72	Thyroid 3 grains, stopped 6/19/36
7/16/36	180½	108/ 70	Hypoglycemic reaction; diet: calories 800; carbohydrate 100, protein 80, fat 20
8/ 7/36	.....	.....	Diet: Calories 750; carbohydrate 70, protein 75, fat 20
9/25/36	177½	.....	
10/27/36	.....	.....	Plastic operation
11/17/36	156½	.....	Discharged

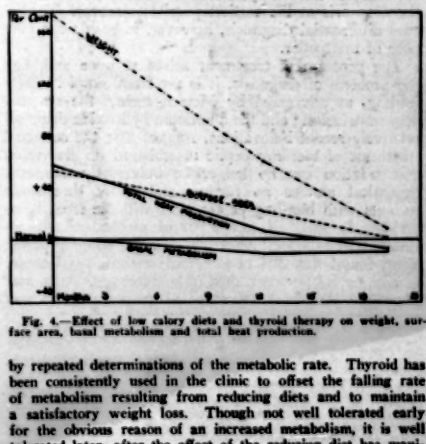

Fig. 4.—Effect of low calory diets and thyroid therapy on weight, surface area, basal metabolism and total heat production.

1. Evans, F. A., and Strang, J. M.: A Departure from the Usual Methods in Treating Obesity, Am. J. M. Sc. **177**: 339 (March) 1929.

2. Short, J. J., and Johnson, H. J.: The Increased Metabolism of Obesity, J. A. M. A. **106**: 1776-1779 (May 23) 1936.

3. Strang, J. M., and Evans, F. A.: The Energy Exchange on Obesity, J. Clin. Investigation **6**: 277 (Oct.) 1928.

Special Clinical Article

GASTRIC HEMORRHAGE

CLINICAL LECTURE AT SAN FRANCISCO SESSION

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Gastric hemorrhage is a dramatic event. When a person vomits bright red blood or passes a large tarry stool and when in either event he experiences the sickening weakness which accompanies hemorrhage, he usually knows what to do. He calls his doctor. Until a few years ago the doctor, with rare exceptions, thought he also knew what to do. He instituted treatment based on starvation and sedation.

I propose to discuss the problem of gastric hemorrhage from the standpoint of treatment, and as a surgeon I shall confine my discussion to the type of hemorrhage for which the value of surgical intervention is becoming recognized, namely bleeding peptic ulcer. Peptic ulcer, according to Bulmer,[1] causes 89 per cent of acute hemorrhages from the upper part of the intestinal tract, 5.3 per cent of such hemorrhages being caused by esophageal varices and 1.5 per cent by gastric carcinoma. Owen,[2] in studying 137 cases of gross and massive hemorrhage from the intestinal tract at the Philadelphia General Hospital, found that 68 per cent of the hemorrhages were caused by peptic ulcer, 25 per cent by gastric carcinoma and 6 per cent by varices or carcinoma of the esophagus.

That bleeding ulcers give rise to the majority of gastric hemorrhages and hemorrhages from the upper part of the intestinal tract is clear. That the differential diagnosis between peptic ulcer, carcinoma of the stomach, gastritis and the varices of cirrhosis or splenomegaly can be far from simple is perhaps not so well appreciated. It is important, nevertheless, to establish the diagnosis at the earliest possible moment. To discuss differential diagnosis, however, is beside the purpose of this paper.

The problem of treatment arises at once and, like the problem of diagnosis, it is far from simple. Early feeding, as advocated by Meulengracht,[3] the massive drip transfusion [4] and the aluminum hydroxide drip,[5] all relatively recent innovations, suggest that the standard treatment of bleeding peptic ulcer based on starvation and sedation can no longer be universally accepted. Statistical studies go further and show that some patients with bleeding peptic ulcer will die from hemorrhage in spite of any form of medical treatment. Emery and Monroe,[6] reporting on 1,435 cases of peptic ulcer, found that 384 of their patients bled. Of these, twenty, or 5.2 per cent, died of hemorrhage. Allen and Benedict [7] studied 1,804 cases of duodenal ulcer and found that 30 per cent of the patients bled. Of this number 138 had sudden severe hemorrhages, and for them the mortality was 14.5 per cent. Owen cited a mortality of 6 per cent in 137 cases of gross and massive hemorrhage from peptic ulcer. Twenty-six of his patients had massive hemorrhage from duodenal ulcer and six of these died, giving a mortality of 23 per cent, a figure which emphasizes the danger to life of massive hemorrhage from duodenal ulcer. Bulmer cited a mortality of 10 per cent, Hinton [8] of 11 per cent and Lahey [9] of 5 per cent. In contrast to these figures, Hurst and Ryle [10] reported a mortality from hemorrhage of 3 per cent in private practice and 4.8 per cent in hospital ward practice. Meulengracht reported a mortality of 1.3 per cent with his plan of feeding, his previous mortality with the old regimen of starvation and sedation having been 7.9 per cent. When one analyzes his reports, it would appear that his series is not strictly comparable with the cases of massive hemorrhage with possible surgical implications which are being considered here. His plan cannot yet be recommended.

Such varied mortality rates are puzzling until one remembers that, as Means [11] said, ". . . hemorrhage occurs under a variety of circumstances having different therapeutic significance. There are large exsanguinating hemorrhages; there are small ones carrying little risk. There are first hemorrhages and recurrent hemorrhages. There are hemorrhages in young persons and in old. All these factors have to be taken into consideration in planning treatment."

It seems fair to state that the mortality from massive hemorrhage complicating peptic ulcer, in this country at least, is 5 per cent or more with medical treatment. The mortality from massive hemorrhage complicating duodenal ulcer is definitely higher. The only hope for certain patients lies in early operation.

The attitude of the surgeon toward this complex and interesting problem should be characterized by a desire for close cooperation with the medical man in every case of hemorrhage. Patients should be hospitalized. All efforts should be made to arrive at a prompt and accurate diagnosis. In each case a decision as to whether the patient should be treated medically or whether surgical intervention alone can save him should be made within Finsterer's [12] time limit of from twenty-four to forty-eight hours from the onset of bleeding. The few patients who can be saved only by operation must be operated on early if they are to have every chance.

In making decisions of this nature, one can be guided somewhat by a few established facts. The incidence and the mortality of hemorrhage from ulcer is greater for men than for women. The incidence and the mortality of hemorrhage rise with age and with the presence of arteriosclerosis and hypertension. Hemorrhage from duodenal ulcer carries a higher mortality than hemorrhage from gastric ulcer. Hemorrhage from chronic ulcer is more likely to be fatal than hemorrhage from acute ulcer. Mortality rises rapidly with a second

Read in the Surgical Division of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1938.

1. Bulmer, Ernest: Mortality from Hematemsis, Lancet **2**:720 (Oct. 1) 1932.
2. Owen, H. R.: Personal communication to the author.
3. Meulengracht, E.: Weitere Erfahrungen über die Behandlung massiver Magenblutungen ohne Beschränkung der Nahrungszufuhr, München. med. Wchnschr. **49**:1565 (Oct. 1) 1937.
4. Marriott, H. L., and Kekwick, A.: Continuous Drip Blood Transfusion, Lancet **1**:977 (April 27) 1935.
5. Waldman, E. E.: The Treatment of Hematemesis and Melena by a Continuous Aluminum Hydroxide Drip, Am. J. M. Sc. **194**:333 (Sept.) 1937.
6. Emery, E. S., and Monroe, R. T.: Peptic Ulcer—Nature and Treatment, Based on a Study of 1,435 Cases, Arch. Int. Med. **55**:271 (Feb.) 1935.
7. Allen, A. W., and Benedict, E. B.: Acute Massive Hemorrhage from Duodenal Ulcer, Ann. Surg. **98**:736 (Oct.) 1933.
8. Hinton, J. W.: Fatal Hemorrhage in Peptic Ulcer Treated Conservatively, Am. J. Surg. **22**:315 (Nov.) 1933.
9. Lahey, F. H.: Peptic Ulcer, Pennsylvania M. J. **41**:79 (Nov.) 1937.
10. Hurst, A. F., and Ryle, J. A.: The Incidence, Mortality and Treatment of Hemorrhage in Gastric and Duodenal Ulcer, Lancet **1**:1 (Jan. 2) 1937.
11. Means, J. H.: Treatment of Peptic Ulcer: Indications for Surgery, Surg., Gynec. & Obst. **66**:264 (Feb., No. 2 A) 1938.
12. Finsterer, Hans: Die operative Behandlung der akuten profusen Magen- und Duodenalblutungen, Wien. klin. Wchnschr. **44**:1125 (Sept. 25), 1160 (Sept. 11), 1185 (Sept. 18) 1931; Operative Treatment of Severe Gastric Hemorrhage of Ulcer Origin, Lancet **2**:303 (Aug. 6) 1936.

or third massive hemorrhage closely following initial bleeding. According to Gordon-Taylor [13] the mortality from such a second hemorrhage is from 74 to 78 per cent. With regard to patients who survive, Lahey stated that 40 per cent of patients who have bled once will not be relieved of ulcer symptoms by medical treatment and that 80 per cent of patients who have bled two or more times will not be relieved of ulcer symptoms by medical treatment.

TABLE 1.—*Incidence of Hemorrhage*

	No. of Cases	Percentage
Total number of cases of ulcer	343	..
Perforation	81	24
Gross hemorrhage	62	18

TABLE 2.—*Distribution of Bleeding Ulcers*

	No. of Cases	Percentage
Hemorrhage from duodenal ulcer	44	71
Hemorrhage from gastric ulcer	15	24
Hemorrhage from anastomotic ulcer	3	5

The mortality figures for surgical intervention vary greatly. However, when technic is fairly uniform, the principal factor which influences mortality is the time interval between the onset of hemorrhage and operation. Finsterer has demonstrated that the time element is all important. With thirty-five early resections for massive bleeding he had one death, or a mortality of 2.8 per cent; with forty-two late resections for massive hemorrhage he had thirteen deaths, or a mortality of 31 per cent. Resection is not always possible or necessary. With forty-two early operations of various types, all for severe bleeding, Finsterer had two deaths, or a mortality of 4.8 per cent. He maintained that this is the only fair figure to compare with mortality rates for medical treatment, for early operation means operation within twenty-four to forty-eight hours of the initial bleeding. What is more, this figure must be compared with the mortality for medical treatment in cases of massive hemorrhage and not with the rate for such treatment in general groups of consecutive cases.

The cases I shall report are consecutive cases of severe hemorrhage complicating peptic ulcer which were observed at the Lankenau Hospital during the past four years and at the Abington Memorial Hospital during the past twelve years. Only cases of gross hemorrhage, such as copious hematemesis or melena, frequently associated with syncope and always associated with weakness and a marked fall in the hemoglobin content and red count are included. Four surgeons and twelve medical men handled the patients. While the series is small, it throws some light on the incidence of ulcer complications in private patients and the better class of ward patients.

Table 1 shows the incidence of perforation and gross hemorrhage in all patients admitted during the time covered by this study.

Table 2 shows the distribution of the bleeding ulcers. As in most series, duodenal ulcer was the most frequent site of hemorrhage. Two of the anastomotic ulcers were jejunal, one occurring after a gastroenterostomy performed eleven years previously and the other after a pylorectomy performed nineteen years previously. The third was gastric, occurring at the site of a sleeve resection done eight years previously.

Table 3 is a comparison of mortality rates with medical and with surgical treatment. The general mortality is 12.9 per cent, the mortality with medical treatment 7.5 per cent and the mortality with surgical treatment 22.7 per cent. Obviously the mortality with operation is higher than it should be. Twelve of the twenty-two operations were on patients who came to operation as medical failures, for whom the surgeon was first called in five or more days after the initial hemorrhage, often after one or more successive hemorrhages, and usually in the face of continued bleeding. Four of these twelve died, and the resulting mortality of 33 per cent represents the mortality for surgically treated medical failures. In the ten cases in which operation was the procedure of election, the only fatality resulted from bundle branch block, which developed on the eighth postoperative day during an otherwise smooth convalescence.

Table 4 is an analysis of the fatalities. The eight patients who died were all men. All but one were over 40. Five had duodenal and three had gastric ulcer. Without more detailed analysis, it may be noted that two fatalities resulted from radical operation for ulcer, two after indirect attack for ulcer and only one when the attack was made directly on the bleeding in the simplest operative fashion. In the last-mentioned case death resulted from bundle branch block after eight days of apparently uncomplicated postoperative recovery.

Table 5 shows the results of a follow-up study of the cases in which treatment was medical. Salient points are the few patients who completely recovered, the number of patients who had symptoms of ulcer and three cases of recurrent bleeding. The patients who

TABLE 3.—*Mortality Figures*

	All Patients	Patients Medically Treated	Patients Surgically Treated
Number of patients	62	40	22
Deaths	8	3	5
Mortality	12.9%	7.5%	22.7%

TABLE 4.—*Fatalities*

Medical—3	
Hemorrhage	duodenal
Hemorrhage	gastric
Hemorrhage plus pneumonia	duodenal
Surgical—5	
Hemorrhage following excision of ulcer	gastric
Hemorrhage following pyloroplasty	pyloric
Pneumonia following resection	duodenal
Pneumonia following pyloroplasty	duodenal
Bundle branch block, heart failure	duodenal
Operation: suture at base of ulcer, oversewing of duodenal wall	

bled were men aged 57, 62 and 64, all with duodenal ulcer, and the last of these died of recurrent hematemesis thirteen months after discharge.

Table 6 is a follow-up study of the cases in which treatment was surgical. Points of interest are the high percentage of patients who recovered from all symptoms of ulcer and the two cases of recurrent bleeding. Of the eleven recoveries, six were after pyloroplasty combined with cauterization or suture of the ulcer,

13. Gordon-Taylor, Gordon: The Problem of the Bleeding Peptic Ulcer, Brit. J. Surg. 25:403 (Oct.) 1937.

three were after posterior gastro-enterostomy and two were after gastric resection. At operation on one of the patients who bled after discharge from the hospital, a large ulcer was found near the common duct complicated by diffuse cholecystitis and chronic catarrhal appendicitis. The gallbladder and appendix were removed in the hope that the ulcer would then subside with medical treatment. Two months after discharge the patient died of hematemesis. This was an early

TABLE 5.—*Follow-Up After Medical Treatment (Twenty-Six of Thirty-Seven Cases, or 70 Per Cent, Traced)*

Result	No. of Cases	Percentage	Percentage of Traced Cases
Complete recovery	10	27	39
Mild indigestion	7	18	27
Severe indigestion	5	14	19
Recurrent bleeding	3	8 (1 died)	11
Died, other causes	1	3	4

case, that of a man aged 39, and taught me to attack bleeding ulcers directly. The other patient with recurrent bleeding was a man aged 53 on whom pyloroplasty was performed for pyloric ulcer. Because of the recurrent bleeding, subtotal gastrectomy was advised.

From this series I have learned several lessons. Additional support is given to the fast accumulating evidence that an appreciable number of patients with bleeding ulcer will die of exsanguination with medical treatment alone. Fully realizing that most patients with initial hemorrhage recover with medical treatment, one must realize also that a certain percentage can be saved only by operation. Every patient with severe hematemesis or melena should therefore be hospitalized at once, and on arriving at the hospital the patient should be seen by a medical man and by a surgeon. The diagnosis of ulcer may have been made prior to hemorrhage or may be clear from the history. If not, the necessary and practicable steps should be taken to make it. Unless the bleeding continues unabated, barium sulfate may be given by mouth to aid in diagnosis. The danger in this procedure is not in the giving of the drug but in the transportation of the patient to the x-ray room and in the leaded glove of the examiner. Transportation should be done with care and deep palpation of the abdomen should be forbidden. The patient should be kept recumbent.

Within the first twenty-four hours every effort should be made to judge whether or not the individual is of the group of patients who are not likely to recover with medical treatment. According to Allen and Benedict the eventual survivors pick up rapidly after their first prostration. The prediction as to survival should be based on the severity and duration of bleeding, the patient's reaction to that bleeding, the patient's age and sex and the presence or absence of vascular disturbances. Allen [14] expressed the belief that the age of the patient has more bearing on the cessation of hemorrhage than any other factor, the mortality increasing greatly for patients over 50. The cases just cited indicate that patients between 40 and 50 should also be included in the dangerous group. Jones [15] suggested transfusions as an index to whether or not bleeding will continue. He pointed out that with each transfusion the beneficial effect of blood is less and said that, if a second transfusion is necessary within forty-eight or seventy-two hours, one should transfuse and operate.

14. Allen, A. W.: Acute Massive Hemorrhage from the Upper Intestinal Tract, Surgery **2**:713 (Nov.) 1937.
15. Jones, D. F., in discussion on Allen and Benedict.[14]

OPERATION

I believe that there are three groups of patients for whom operation is indicated. The first is that group with sudden massive hemorrhage who, according to the criteria just reviewed, are very likely to die with expectant or medical treatment. The second is the group who have severe recurrent bleeding with medical treatment. The third is the group who have recovered from an episode of hemorrhage but who continue to have symptoms of indigestion and high acidity or continued lesser bleeding in spite of medical treatment. Let me emphasize that, with each of these groups, after operation has been performed management along medical lines must continue indefinitely.

If early operation for bleeding is to be done, it should be performed only in cases of definite ulcer. Massive hemorrhage in a man over 50 who is known to have an ulcer and who does not rally soon after the initial hemorrhage is the most obvious indication. With the acute bleeding which occasionally is the first sign of ulcer but may be due to other lesions, the experience and judgment of the medical man and the surgeon conjointly must answer the question. When operation is undertaken, it should be done early, within twenty-four to forty-eight hours after the onset of bleeding, and it should be done with the sole intention of controlling the bleeding directly. By direct attack on the source of bleeding is meant direct localization and exposure of the ulcer, whether gastric or duodenal. At the time of operation one should give massive blood transfusion. In the more fortunate cases immediate resection, which includes the ulcer, may be done without greatly increasing the risk of operation. Surgical judgment is in the highest degree necessary. The important point is to regard the condition as an emergency requiring safe and immediate control of hemorrhage as a complication of ulcer rather than as an ulcer requiring radical operation for its cure. I have previously called attention to the value of anterior gastroduodenotomy in locating the source of hemorrhage at the operating table.[16] The following is a typical case:

TABLE 6.—*Follow-Up After Surgical Treatment (Sixteen of Seventeen Cases, or 92 Per Cent, Traced)*

Result	No. of Cases	Percentage	Percentage of Traced Cases	Operation
Complete recovery	11	65	73	Pyloroplasty 6 Posterior gastro-enterostomy 3 Gastric resection 2
Mild indigestion	1	6	7	Pyloroplasty
Severe indigestion	1	6	7	Posterior gastro-enterostomy, cauterization, ulcerated duodenum, hemangioma
Recurrent bleeding	2	12	13	Cholecystectomy, appendectomy, pyloroplasty

CASE 1.—A large duodenal ulcer, almost 1 inch in diameter, was situated on the posterolateral duodenal wall. The patient had had two previous operations without the ulcer's being located. Over a period of eleven years he had bled severely on numerous occasions. The last two almost lethal hemorrhages had occurred within a period of three months. By

16. Pfeiffer, D. B.: Massive Hemorrhage from Posterior Duodenal Ulcer, Ann. Surg. **103**:473 (March) 1936.

gastroduodenotomy a low posterior ulcer was found, an exposed vessel in the bed was sealed by electrocautery, the bed was cauterized, the craggy edges were nicked circumferentially and the operation completed as a wide pyloroplasty. The patient made an uncomplicated recovery and was free from bleeding or symptoms of ulcer four years later.

I repeat that, as a rule, I believe that the bleeding patient should not be subjected to too much surgical procedure. While the ulcer is bleeding is the time for the saving of life, not for the curing of the ulcer. The situation is somewhat similar to that in which operation is performed for intestinal obstruction due to colonic growths when obstruction is relieved at primary operation and the growth is later removed. The objective in the cases under discussion is hemostasis. Gastrotomy or duodenotomy will usually provide access to the ulcer. In the ulcer bed the actual bleeding point can frequently be found. The point may be sealed with the ball electrode, and an encircling stitch of chromic catgut may be placed through the tissues above and below. If the point is not discovered, similar procedures may still be adopted and it may be possible to mobilize overhanging edges and bring them together by suture. Small radiating incisions may be of advantage in the case of a large excavated ulcer. It is impossible to enumerate the precise procedures adapted to the varying individual cases, but it is important that uppermost in the surgeon's mind should be the immediate objective of controlling hemorrhage and not the ultimate desideratum of cure of the ulcer. A great advantage of anterior gastroduodenotomy for posterior ulcer is the opportunity afforded by it to terminate the operation as a gastroduodenostomy. While this procedure is not recommended as a definitely curative operation for ulcer, it would seem to be that in many instances. The mortality with such a procedure is extremely low. It may be done without exceeding the vitality of an exsanguinated patient, and it does not interfere with a subsequent radical operation should that be considered wise.

A case illustrative of these principles was observed at the Abington Memorial Hospital three weeks ago, too late to be included in the statistics just presented:

CASE 2.—A man aged 50, who had epigastric pain and vomiting characteristic of peptic ulcer for several days, in 1919 had a posterior gastro-enterostomy at another hospital for duodenal ulcer. The morning of admission he passed a large tarry stool, and he was admitted to the hospital in a state of shock. He rallied fairly well, but the next morning he vomited a large amount of bright red blood and again went into shock. The blood pressure fell to 80/30. The hemoglobin content was 55 per cent and the red count 3,200,000. Operation with massive transfusion was performed a few hours later. A gastrotomy gave ready access to a gastrojejunal ulcer with an open vessel in the bed. The ulcer was partially excised within the stomach and bleeding was stopped. The patient's convalescence has been perfectly smooth.

In cases in which bleeding has been controlled with medical treatment, operation must be considered because of the likelihood of another hemorrhage in the future. Here judgment is essential. Recurrent bleeding with medical treatment indicates progression of the ulcer, and operation should be performed. Subtotal gastrectomy with removal of the ulcer is usually the best curative procedure.

When bleeding has been controlled by medical measures but pain due to ulcer and high acidity persist in spite of treatment, resection should also be considered.

CONCLUSION

The treatment of gastric hemorrhage caused by a bleeding peptic ulcer is a complicated problem which calls for the pooled resources and close cooperation of the medical man and the surgeon.

A certain number of patients with bleeding ulcer will die with medical treatment. Every effort should be made to single these patients out and to give them the benefit of early operation.

At operation for bleeding ulcer, the primary consideration is hemostasis. After operation continued medical care should be the rule, and in selected cases more extensive surgical procedure should be considered.

1822 Pine Street.

Council on Pharmacy and Chemistry

ERGONOVINE

Report of the Council on Pharmacy and Chemistry

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT, WHICH HAS KINDLY BEEN PREPARED FOR THE COUNCIL BY DR. RALPH G. SMITH.

PAUL NICHOLAS LEECH, Secretary.

THE PRESENT STATUS OF ERGONOVINE

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The recent discovery of a new and pharmacologically potent alkaloid of ergot has aroused considerable interest both in purely scientific and in clinical circles. Certain factors which have stimulated such interest are as follows: It is characterized by a number of physical, chemical and pharmacologic properties which differ decidedly from those of the previously known alkaloids of ergot, all of which show considerable similarity. Although hitherto unrecognized, it apparently plays an important role in the clinical oxytocic activity of those preparations of ergot which contain it and in the purified form is proving itself to be a valuable drug in the practice of obstetrics. Furthermore, the closely consecutive publications of its discovery from various laboratories naturally initiated discussion regarding priority.

As sufficient time has elapsed since the first announcements for general agreement on the properties of the alkaloid and for some indication of its therapeutic application, it is possible to describe its characteristics with a minimum of controversial discussion. However, before proceeding to that phase of the subject it might be of interest to review briefly the publications concerned with its early development.

Chassar Moir [1] in 1932, by means of the intra-uterine rubber bag method of Bourne and Burn,[2] recorded uterine contractions and tonus changes following the administration of various ergot preparations to puerperal patients. Several samples of B. P. liquid extracts

From the Laboratory of Pharmacology, University of Michigan Medical School.

1. Moir, Chassar: The Action of Ergot Preparations on the Puerperal Uterus, Brit. M. J. 1:1119-1122 (June 18) 1932.
2. Bourne, Aleck, and Burn, J. H.: The Dosage and Action of Pituitary Extract and of the Ergot Alkaloids on the Uterus in Labor, with a Note on the Action of Adrenalin, J. Obst. & Gynaec. Brit. Emp. 34: 249-268, 1927.

of ergot, prepared by aqueous extraction and containing only traces of the known ergot alkaloids, invariably produced, in 2 drachm (7.5 cc.) doses, a decided response which was more marked, especially with regard to tonus increases, than that produced by pure ergotoxine or ergotamine preparations administered by mouth or even by intramuscular injection. It having also been demonstrated that the activity of the liquid extracts could not be explained by their histamine or tyramine content, the action was ascribed to some still unknown factor.

Swanson and Hargreaves [3] in 1934 reported the comparative effect, as recorded by an intra-uterine rubber balloon, of various ergot preparations on the intact puerperal uteri of etherized dogs. On oral administration certain extracts and fluidextracts of ergot produced a definite response in from four to twenty minutes, while comparable doses, as determined by the cock's comb assay method, of ergotamine tartrate and ergotoxine ethanesulfonate brought about a similar effect only in from thirty to sixty minutes. Little difference in the various preparations was detected on intravenous administration. The conclusion reached was that "ergot contains a principle (not ergotamine or ergotoxine) that produces by mouth a rapid onset of action on the puerperal uterus of dogs."

Early in 1935 certain papers appeared from various sources which confirmed and extended these observations. Thompson [4] in January and March reported a study of various ergot preparations and fractions as recorded from the exposed uterus of the lightly anesthetized pregnant cat. (The two papers were previously presented at meetings of the American Pharmaceutical Association in August 1932 and May 1934 respectively.) According to the January report, hydro-alcoholic and aqueous extracts of ergot were prepared, containing the alkaloidal equivalent in 1 cc. of 0.5 mg. and 0.19 mg. respectively of ergotoxine ethanesulfonate as assayed by the Broom-Clark and cock's comb methods. These extracts produced a similar response, usually within ten minutes, in contrast to equivalent amounts of ergotoxine and ergotamine salts, which were more weakly effective and only in from thirty to sixty minutes after oral administration. Such results confirmed the work of Moir, suggesting the presence of some unknown potent principle which was considered as alkaloidal in nature. In the March paper were reported the method of separation of the new active substance in an amorphous form and certain of its properties, its smaller molecule and its greater solubility in water and numerous organic solvents in comparison with other ergot alkaloids being recognized. From the pharmacologic description, a very crude preparation was obviously concerned but a footnote reported its isolation in crystalline form. Thompson [5] later stated that the footnote was in the paper at the time of its submission for publication in May 1934 and in his doctorate dissertation, submitted before that time; also that the isolation in crystalline form was reported at the American Pharmaceutical Association meetings in May 1934 and that in the same month the name "ergostetrine" was assigned in a U. S. patent application. In a paper delivered in April 1935 at a meeting of the American Society for Pharmacology and Experimental Therapeutics the alkaloid was referred to as ergostetrine, but in an abstract [6] of this paper published in June 1935 it is still called "X" alkaloid. The method of isolation appeared in September 1935.[7] Koff [8] reported in February 1935 a clinical investigation of ergot preparations by the intra-uterine balloon method, confirming Moir's conclusions regarding an unknown active substance in ergot. Also, on examination of Thompson's extracts he found the activity to lie wholly in the alkaloidal fraction, which still showed similar effects after removal of the ergotoxine group of alkaloids.

A publication by Davis, Adair, Rogers, Kharasch and Legault [9] appeared in February 1935 (previously presented at a meeting of the Central Association of Obstetricians and Gynecologists in November 1934) reporting the extraction of a water and alcohol soluble fraction from ergot which was considered to be non-alkaloidal on the basis of certain properties not characteristic of the known ergot alkaloids. This fraction in 3 mg. doses by mouth in more than 100 cases produced an increase in rhythm and tone in the quiescent puerperal uterus, beginning in fifteen minutes and persisting for from three to four hours after administration, as recorded by the intra-uterine balloon method. On the contrary, ergotamine, ergotoxine and sensibamine (now believed to be an equimolecular combination of ergotamine and ergotaminine [10]) in 3 mg. doses by mouth produced no effect over a period of one hour. The experiments here described were carried out with an impure substance, but in a footnote it was stated that the active principle had been isolated in crystalline form. In another footnote it was reported that a commercial firm had consented to make large quantities of the substance for clinical assay and had given it the name "ergotocin." The impression is given that "ergotocin" referred to the impure product, but Kharasch and Legault later state, in publications describing certain properties and clinical effects of the pure substance, that it referred to the crystalline product which had been obtained in December 1934 [11] and which Eli Lilly & Co. had been preparing for two months and with which they had records on more than 200 patients.[12] A photomicrograph of the needle-shaped crystals of ergotocin, isolated by Kharasch, appeared on the cover of the March 1935 *Journal of Chemical Education*.[13] The empirical formula $C_{21}H_{27}O_3N_3$ (which included a molecule of ethyl alcohol), assigned to the alkaloid by Kharasch and Legault, was published in June 1935.[14] The study of the chemistry of ergot was apparently begun by Kharasch and Legault early in 1932.[15]

3. Swanson, Edward E., and Hargreaves, Chester C.: The Action of Ergot and Its Alkaloids on the Puerperal Uteri of Dogs, J. Am. Pharm. A. **23**: 867, 1934.

4. Thompson, Marvin R.: The Active Constituents of Ergot: A Pharmacological and Chemical Study, J. Am. Pharm. A. **24**: 24-38 (Jan.), 185-196 (March) 1935.

5. Thompson, Marvin R.: The New Active Principle of Ergot, Science **81**: 636-639 (June 28) 1935.

6. Thompson, Marvin R.: The Active Principles of Ergot, J. Pharmacol. & Exper. Therap. **54**: 161 (June) 1935.

7. Thompson, Marvin R.: Some Properties of Ergostetrine, J. Am. Pharm. A. **24**: 748, 1935.

8. Koff, Arthur K.: A Study of the Action of Ergot on the Human Puerperal Uterus, Surg., Gynec. & Obst. **60**: 190 (Feb.) 1935.

9. Davis, M. E.; Adair, Fred L.; Rogers, Gerald; Kharasch, M. S., and Legault, Romeo R.: A New Active Principle in Ergot and Its Effect on Uterine Motility, Am. J. Obst. & Gynec. **29**: 155-167 (Feb.) 1935.

10. Stoll, Arthur; Rothlin, E.; Löffler, W., and Dale, Sir Henry: Die Pharmakologie des Mutterkorns, Schweiz. med. Wchnschr. **65**: 1077-1082 (Nov. 9) 1935.

11. Kharasch, M. S., and Legault, R. R.: Ergotocin, Science **81**: 388 (April 19) 1935. Ergotocin: The Active Principle of Ergot Responsible for the Oral Effectiveness of Some Ergot Preparations on Human Uteri, J. Am. Chem. Soc. **57**: 956 (May) 1935.

12. Kharasch, M. S., and Legault, R., R.: Ergotocin, Lancet **1**: 1243 (May 25) 1935; footnote 14, first reference.

13. The explanation appeared in the May issue, p. 238.

14. Kharasch, M. S., and Legault, R. R.: The New Active Principle(s) of Ergot, Science **81**: 614-615 (June 21) 1935; footnote 44, first reference.

15. Adair, Fred L.; Davis, M. E.; Kharasch, M. S., and Legault, R. R.: A Study of a New and Potent Ergot Derivative (Ergotocin), Am. J. Obst. & Gynec. **30**: 466 (Oct.) 1935; **30**: 740 (Nov.) 1935.

The first detailed description of the method of preparation, physical properties and results of chemical analysis of the crystalline form of the new alkaloid, which they named "ergometrine" was published by Dudley and Moir[16] in March 1935. The analytic results were presented with reservation to allow slight modification after more drastic purification and no empirical formula was suggested at this time. Some modification of the analytic results and also of the physical properties was later found to be necessary. In the same paper, clinical results as recorded by the intra-uterine bag method and also by extra-abdominal recording apparatus were presented showing stronger and more prompt uterine activity on administration of the new alkaloid by mouth, intramuscularly or intravenously than that produced by the previously known ergot alkaloids. The former was also free from undesirable side actions. Some of the pharmacologic observations of Brown and Dale, such as the practical absence of epinephrine inhibiting effect, were included. The description of a method of preparation suitable for large scale operation was published later.[17]

In May 1935 Stoll and Burckhardt[18] reported the isolation in crystalline form of a new ergot alkaloid which they named "ergobasin" (referring to its comparatively strong basic reaction in aqueous solution), described the method of preparation and certain of its physical and chemical properties and presented photomicrographs of the crystals of the alkaloid and of certain of its salts. (It was later stated[19] that ergobasine had been prepared at the beginning of 1935.) On the basis of their analyses the empirical formula was announced as $C_{19}H_{22}O_2N_2$, which was confirmed by Jacobs and Craig,[19] who reported in July 1935 the isolation of the same alkaloid. The same formula was later accepted by Dudley,[20] by Davis, Adair and Pearl[21] and by Thompson.[7]

As a result of this contemporaneous work and the announcement in close succession of the isolation of the new alkaloid by four laboratories in Europe and America, considerable discussion naturally arose regarding priority.[22] At least a part of the confusion resulted from the uncertainty that all workers had isolated the same principle, since the initial announcements concerned preparations not absolutely pure and consequently differing slightly in physical constants and chemical properties. An exchange of samples among the four laboratories resulted in a mutual publication early in 1936 by Kharasch, King (in place of Dudley, then deceased), Stoll and Thompson[23] to the effect that ergometrine, ergotocin, ergobasin and ergostetrine were the same substance and that the four names were synonymous. A detailed report of the comparison as carried out by Stoll and Burckhardt was later published.[24] Chen, Swanson, Kleiderer and Clowes[25] in a comparison involving action on the isolated rabbit uterus, the cock's comb and the *p*-dimethylamino benzaldhyde reactions and combustion analyses reached the same conclusion. Thompson[26] also reported identity on the basis of physical and pharmacologic characteristics.

On March 14, 1936, the Council on Pharmacy and Chemistry of the American Medical Association adopted the name "ergonovine" for the new ergot alkaloid,[27] since all of the names mentioned were either considered therapeutically suggestive (ergotocin, ergostetrine, ergometrine) or were proprietary (ergotocin, ergostetrine, ergobasin). Although the Council concedes to the discoverer the right to a proprietary name, in order to avoid confusion it is the policy to recognize only one such name for the same substance. In this case it was unable to establish undisputed priority so decided to allow no proprietary name. The action of the Council stimulated certain adverse criticism.[28] The names "ergometrine" and "ergobasin" are still being used in Europe.

Regarding priority, it is of interest that on June 13, 1932, about one week before the appearance of Moir's early paper,[1] Elmer H. Stuart of the Eli Lilly Company made U. S. patient application for an ergot-derived product and a process for obtaining it. This product was conceded to be a mixture but from its peculiar optical rotation ($[\alpha]_D^{25°} = -34°$) in chloroform it was argued that it contained an alkaloid not hitherto described, in addition to ergotoxine and ergotamine, and having similar physiologic properties. In an amendment filed March 24, 1933, the high potency on the puerperal uterus in comparison to ergotamine and ergotoxine was stressed. From time to time patent claims were extended to cover properties as they were discovered, mostly by other investigators, which were confirmed for this mixture or for ergonovine separated from it. A patent covering all these properties was finally granted, Jan. 12, 1937. However, the Council on Pharmacy and Chemistry refused the claim, on the basis of this patent, of the Eli Lilly Company to the right of a proprietary name for the purified alkaloid, in that Stuart was not the first one to isolate it or to distinguish clearly its most important medical properties.

PHYSICAL AND CHEMICAL PROPERTIES

The alkaloidal base ergonovine is a colorless, tasteless, odorless, crystalline substance, appreciably soluble in water (1:200-300 at 20 C.[18]), showing in solution a weak but definitely alkaline reaction[29] and a bluish fluorescence.[30] In dilute aqueous solutions of organic and mineral acids it dissolves very readily.[31] It is freely

16. Dudley, H. W., and Moir, Chassar: The Substance Responsible for the Traditional Clinical Effect of Ergot, Brit. M. J. 1: 520 (March 16) 1935.

17. Dudley, Harold W.: The Preparation of Ergometrine, Pharmaceut. J. 134: 709 (June 15) 1935.

18. Stoll, Arthur, and Burckhardt, Ernst: L'ergobasine, un nouvel alcaloïde de l'ergot de seigle soluble dans l'eau, Compt. rend. Acad. d. sc. 200: 1680-1682 (May 13) 1935; Bull. d. sc. pharmacol. 42: 257-266 (May) 1935.

19. Jacobs, Walter A., and Craig, Lyman C.: On an Alkaloid from Ergot, Science 82: 16-17 (July 5) 1935.

20. Dudley, H. W.: The Relationship of Ergotocin to Ergometrine, J. Am. Chem. Soc. 57: 2009 (Oct.) 1935; footnote 33.

21. Davis, M. Edward; Adair, Fred L., and Pearl, Sarah: The Present Status of Oxytocics in Obstetrics, J. A. M. A. 107: 261-267 (July 25) 1936.

22. Dale, H. H.: The New Ergot Alkaloid, Science 83: 99-101 (Aug. 2) 1935. Stoll, Arthur: The New Ergot Alkaloid, ibid. 82: 415-417 (Nov. 1) 1935. Thompson,[5] Kharasch and Legault, footnote 14, first reference. Dudley and Moir.[16] The Active Oxytocic Principle of Ergot, editorial, J. A. M. A. 104: 1910 (May 25) 1935. The Relationship of the Recently Discovered Ergot Alkaloids.[20]

23. Kharasch, M. S.; King, H.; Stoll, A., and Thompson, Marvin R.: The New Ergot Alkaloid, Science 83: 206-207 (Feb. 28) 1936; Nature 137: 403, 1936; Schweiz. med. Wchnschr. 66: 261 (March 14) 1936.

24. Stoll, Arthur, and Burckhardt, Ernst: Das neue Mutterkornalkaloid, Schweiz. med. Wchnschr. 66: 353-354 (April 11) 1936.

25. Chen, K. K.; Swanson, Edward E.; Kleiderer, E. C., and Clowes, G. H. A.: Ergotocin, Ergometrine, Ergostetrine and Ergobasine, J. Pharmacol. & Exper. Therap. 57: 74 (May) 1936.

26. Thompson, Marvin R.: Some Observations on the Pharmacology of Ergostetrine (Ergometrine, Ergobasine, Ergotocin), J. Pharmacol. & Exper. Therap. 57: 145 (June) 1936.

27. The New Ergot Alkaloid "Ergonovine," Report of the Council on Pharmacy and Chemistry of the American Medical Association on the New Ergot Alkaloid, J. A. M. A. 106: 1008 (March 21) 1936; Science 83: 296-297 (March 27) 1936; Ergonovine, Current Comment, J. A. M. A. 106: 1012-1013 (March 21) 1936.

28. Why Ergonovine? Pharmaceut. J. 136: 397 (April 11) 1936. Council Correspondence with Sir Henry Dale, J. A. M. A. 106: 1969-1971 (June 5) 1937. Stoll.[18]

29. Dudley and Moir.[16] Dudley.[20] Kharasch and Legault.[22] Stoll and Burckhardt.[24] Thompson.[7]

30. Dudley.[20] Stoll and Burckhardt.[24] Thompson.[7] Allport and Crews.[32]

31. Adair, Davis, Kharasch and Legault.[21] Kharasch and Legault.[22] Thompson.[7]

soluble in methyl and ethyl alcohol,[32] ethyl acetate, acetone, methyl ethyl ketone,[33] acetic ether,[18] less so in ether [15] and sparingly soluble in dichlorethylene,[33] benzene [34] and especially in chloroform.[35]

Ergonovine may be crystallized from a number of solvents, possibly most readily from benzene and chloroform, appearing in the form of long fine needles.[36] Characteristic crystallizations from other solvents have also been described.[37] A troublesome characteristic of ergonovine is a tendency for the crystals to retain some of the solvent in their formation and to release it only with comparatively drastic treatment.[38] This phenomenon apparently accounted for the erroneous empirical formula originally assigned by Kharasch and Legault, an equivalent of alcohol being retained in their preparation.[39]

A melting point with decomposition of 159-163 C. includes most of the values reported for the purified product,[40] although one as high as 164 C.[34] has been obtained. The optical activity, including specific rotation values [e. g. $[\alpha]_D^{23} = +86°$ (c = 0.199) in water,[24] $[\alpha]_D^{25} = -44°$ (c = 0.08) in chloroform [41]] which have been used extensively for identification purposes, has been described in numerous publications.[42]

In contrast to the other alkaloids which are precipitated in dilutions of from 1 : 200,000 to 1 : 2,000,000 by Mayer's reagent, ergonovine is not precipitated in dilutions above 1 : 5,000-1 : 10,000.[43]

A variety of crystalline salts have been prepared [44] and their characteristic crystal forms described.[45] The melting points [46] and optical activities have been reported for several of them, all preparations showing dextrorotation.[47] The water solubility of the salts is also high in comparison with other alkaloids of ergot, the maleate being soluble in water to the extent of 2 per cent at 38 C.[48]

Certain observations have been made regarding the stability of various preparations. Although aqueous solutions of the base are slowly oxidized on exposure to air, acquiring a brown color,[49] solutions in dilute polybasic aliphatic organic acids are stable at ordinary temperatures and may be sterilized by boiling at 100 C. without appreciable loss in oxytocic activity and without imparting color to the solution.[15] The salts keep well in the dry state [21] or in solution in ampules,[50] although the heating of solutions of the salts in sealed tubes for any length of time results in decomposition and darkening.[21]

With regard to color tests characteristic of other ergot alkaloids and dependent on the indole nucleus, ergonovine gives positive glyoxylic acid, Keller and *p*-dimethylaminobenzaldehyde reactions.[51] The last reagent, used in the M. I. Smith colorimetric assay method, yields a more intense color with ergonovine than with the ergotoxine-ergotamine group when compared on a weight basis,[52] in keeping with the smaller molecular weight of ergonovine. Hampshire and Page [53] have obtained equivalent results with ergotoxine and ergonovine when compared on a molecular basis. The color produced by ergonovine in this reaction is spectroscopically identical with that produced by ergotoxine under the same conditions.[53] A positive color reaction has also been reported with the Folin-Denis phenol reagent.[55]

As already indicated, ergonovine, $C_{19}H_{23}N_3O_2$, has a definitely smaller molecule than ergotoxine, $C_{35}H_{39}O_6N_5$, and other alkaloids of ergot with the exception of ergomonamine.[56] On alkaline hydrolysis, it resembles the other alkaloids in yielding lysergic acid [57] but differs from them in the remaining part of the molecule. In the case of ergonovine this consists of a single and comparatively simple radicle *d*-2-amino propanol-1 (CH_3-$CH.NH_2$-CH_2OH).[58]

It is of interest that Smith and Timmis [59] have isolated from ergot and described the properties of an isomer of ergonovine (ergometrine) which they have named ergometrinine. This has been confirmed by Stoll,[60] ergobasinin. This alkaloid, in its physical properties, more closely resembles the older group of ergot alkaloids than does ergonovine. By suitable treatment these two alkaloids are interconvertible and constitute a pair of isomers corresponding to the pairs of previously known alkaloids ergotoxine ergotinine, ergotamine ergotaminine and the still more recently isolated ergosine ergosinine [61] and ergocristine ergocristinine.[62]

32. Dudley.[33] Stoll and Burckhardt.[35] Thompson.[7] Adair, Davis, Kharasch and Legault.[15]
33. Dudley, Harold W.: Ergometrine, Proc. Roy. Soc., London, s. B. **118**: 478-484 (Oct. 3) 1935.
34. Dudley.[36] Thompson.[7] Adair, Davis, Kharasch and Legault.[15]
35. Stoll and Burckhardt.[35] Thompson.[7] Dudley.[36]
36. Adair, Davis, Kharasch and Legault.[15] Davis, Adair and Pearl.[33] Dudley and Moir.[50] Dudley.[36] Stoll and Burckhardt.[35] Thompson.[7]
37. Dudley, H. W.: Properties of Ergometrine, Brit. M. J. **1**: 798 (April 13) 1935. Grant, R. L., and Smith, S.: Dimorphism of Ergometrine, Nature **137**: 154, 1936; Pharmaceut. J. **136**: 146 (Feb. 8) 1936. Dudley and Moir.[50] Stoll and Burckhardt.[35] Dudley.[36] Stoll.[60]
38. Stoll and Burckhardt.[35] Dudley.[36]
39. Davis, Adair and Pearl.[33] Jacobs and Craig.[39]
40. Thompson, Marvin R.: The New Active Principle of Ergot, Science **83**: 62-63 (July 19) 1935. Kleiderer, E. C.: Optical Rotation Study of the New Orally Effective Principle of Ergot, J. Am. Chem. Soc. **57**: 2007 (Oct.) 1935. Adair, Davis, Kharasch and Legault.[15] Dudley.[36] Stoll and Burckhardt.[35] Dudley.[36]
41. Stoll, Arthur: Les alcaloides de l'ergot de Seigle, Bull. d. sc. pharmacol. **45**: 465-490 (Aug.-Sept.) 1936; Die Alkaloide des Mutterkorns, Wien. klin Wchnschr. **49**: 1513-1517 (Dec. 11) 1552-1556 (Dec. 18) 1936.
42. Smith, Sydney, and Timmis, Geoffrey Millward: The Alkaloids of Ergot: Part VII. Isoergine and Isolysergic Acids, J. Chem. Soc., 1936, p. 1440. Bennekou, J., and Schou, Svend A.: Optical Behavior of Ergometrine, Dansk. tids. farm. **10**: 105-108, 1936; Chem. Abstr. **30**: 3044, 1936. Dudley.[36] Stoll and Burckhardt.[35] Jacobs and Craig.[39] Stoll.[41] Kleiderer.[40] Kharasch and Legault, footnote 14, second reference. Adair, Davis, Kharasch and Legault.[15]
43. Stoll and Burckhardt.[35] Kharasch and Legault.[15] Adair, Davis, Kharasch and Legault.[15] Davis, Adair and Pearl.[33]
44. Kharasch, M. S., and Legault, R. R.: Ergotocin, J. Am. Chem. Soc. **57**: 1140 (June) 1935. Dudley.[36] Davis, Adair, Chen and Swanson.[45] Kleiderer.[40] Stoll.[60] Stoll and Burckhardt.[35] Kharasch and Legault.[15] Chen, Swanson, Kleiderer and Clowes.[45] Dudley.[37]
45. Stoll and Burckhardt.[35] Stoll.[60] Kharasch and Legault.[15] Dudley.[37]
46. Dudley.[37] Kharasch and Legault.[15]
47. Dudley.[36] Stoll and Burckhardt.[35] Kleiderer.[40]
48. Davis, M. Edward; Adair, Fred L.; Chen, K. K., and Swanson, Edward E.: The Pharmacological Action of Ergotocine, a New Ergot Principle, J. Pharmacol. & Exper. Therap. **64**: 398-407 (Aug.) 1935.
49. Dudley and Moir.[50] Dudley.[36] Stoll and Burckhardt.[35]
50. Moir, Chassar: Clinical Experiences with the New Alkaloid (Ergometrine), Brit. M. J. **2**: 799-801 (Oct. 24) 1936; Ergometrine, ibid. **2**: 243 (Aug. 1) 1936.
51. Dudley, Harold W., and Moir, Chassar: The New Active Principle of Ergot, Science **81**: 559-560 (June 7) 1935. Austoni, Mario: Methods and Results Obtained in the Determination of Alkaloids of Secale Cornutum, Bol. Soc. ital. sper. **10**: 643-647, 1935. Jacobs and Craig.[39] Dudley.[36] Thompson.[7] Kharasch and Legault.[15] Stoll and Burckhardt.[35]
52. Allport and Crews.[54] Hampshire and Page.[53] Stoll and Burckhardt.[35] Kharasch and Legault.[15] Thompson.[7]
53. Hampshire, G. H., and Page, G. R.: The Chemical Assay of Ergot, Quart. J. Pharm. & Pharmacol. **9**: 60 (No. 1) 1936.
54. Allport, Noel L., and Crews, Sydney K.: Spectrographic Absorption of Ergometrine in Relation to the British Pharmacopeia Color Test, Quart. J. Pharm. & Pharmacol. **8**: 447-452, 1935; Pharmaceut. J. **135**: 5 (July 6) 1935.
55. Kharasch and Legault.[15] Adair, Davis, Kharasch and Legault.[15]
56. Holden, G. W., and Diver, G. R.: A New Alkaloid and an Acid Salt from Ergot, and an Acid Derived from the Salt, Quart. J. Pharm. & Pharmacol. **9**: 230-234 (No. 2) 1936.
57. Jacobs and Craig.[39] Kharasch and Legault.[15]
58. Kharasch, M. S.; Stanger, D. W.; Bloodgood, M. A., and Legault, R. R.: Spectroscopic Similarity Between Ergot (Lysergic Acid) and the Yohimbine Alkaloids, Science **83**: 36-38 (Jan. 10) 1936. Jacobs and Craig.[39]
59. Smith, Sydney, and Timmis, Geoffrey Millward: A New Alkaloid of Ergot, Nature **136**: 259, 1935; Ergometrinine, Pharmaceut. J. **135**: 212 (Aug. 24) 1935; The Alkaloids of Ergot: Part VI, Ergometrinine, J. Chem. Soc. 1166, 1936.
60. Stoll, Arthur: Ergobasine and Its Relation to the Alkaloids of the Ergotamine-Ergotoxine Group, München. med. Wchnschr. **86**: 322-324 (Feb. 26) 1937; footnote 41.
61. Smith, Sydney, and Timmis, Geoffrey Millward: A New Alkaloid of Ergot, Nature **137**: 111, 1936; Pharmaceut. J. **136**: 102 (Jan. 25) 1936; New Alkaloids of Ergot: Ergosine and Ergosinine, Nature **137**: 1075 (June 27) 1936; footnote 61.
62. Stoll, Arthur, and Burckhardt, Ernst: Ergocristin und Ergocristinin, ein neues Alkaloidpaar aus Mutterkorn, Ztschr. f. physiol. Chem. **250**: 1-6, 1937.

(According to Smith and Timmis [63] the ergoclavine of Kussner is a complex of ergosine and ergosinine.) Ergometrinine, like one member in each of the foregoing pairs, is relatively inactive pharmacologically.[64]

A further step in the chemistry of ergonovine is reported by Stoll [65] in that he and Hofmann have synthesized ergobasinin (ergometrinine) from the pharmacologically inactive components lysergic acid and 2-aminopropanol-1 and in turn have converted the former into the pharmacologically active ergobasin (ergonovine).

PHARMACOLOGY

Toxicity.—Ergonovine appears to be from three to four times less toxic in mice, rats and rabbits than ergotamine [66] and ergotoxine.[67] On comparison with ergotamine it is ten times less toxic in the cock, intramuscularly, but of approximately equal toxicity in the cat subcutaneously.[66]

The manifestations produced by poisonous doses resemble those caused by the other alkaloids of ergot and are apparently due in no small part to the lysergic acid component of the molecule, as judged by the toxicity results with ergine, a simple amide of lysergic acid.[69] The most common signs of poisoning in the intact animal, which are essentially due to central action, are excitement, tremors, rapid respiration, weakness of the legs and general weakness, pyrexia, vomiting (in the cat on subcutaneous but not on intravenous injection [67]), convulsions and certain signs of sympathetic stimulation—mydriasis, exophthalmos, retraction of nictitating membrane, erection of the hair, vasoconstriction (ears pale and cold in the rabbit) and tachycardia. As a result of experiments on cats involving adrenalectomies and sympathectomies, Brown and Dale [67] conclude that such signs of sympathetic stimulation are a result to only a minor degree of peripheral action and are chiefly due to central stimulation. In rats the metabolic rate is increased by toxic doses of ergonovine.[66]

In fowl, toxic manifestations on intramuscular injection are also very similar to those produced by ergotoxine but probably less severe (incoordination, depression, dyspnea, staggering gait, drooping wings, salivation, diarrhea and comb changes [67]). The same typical picture, beginning in about five minutes, is produced by ergonovine when administered by mouth, whereas ergotoxine only after forty-five to sixty minutes usually produces a slight effect in comparison with that produced by injection.[67] Although ergonovine produces the characteristic cyanosis of the cock's comb [70] (and rat's tail [71]) there is general agreement that it is much less liable to produce gangrene than is ergotamine and ergotoxine. Also the cyanosis appears somewhat sooner than with ergotoxine and persists for a much shorter time.[67]

Circulatory Effects.—Ergonovine injected intravenously into anesthetized rabbits and spinal cats causes a rise in blood pressure which, in the former animal, is more marked than that resulting from ergotoxine and ergotamine but less so in the latter.[72] In cats anesthetized with chlorbutanol the usual but not invariable effect is a feeble pressor response.[73] In vagotomized dogs under artificial respiration and chloralose anesthesia a strong pressor effect with renal vasoconstriction results.[74] Under evipal, a slight rise in blood pressure with a marked fall in kidney volume occurs.[75] Repeated doses result in a lessened pressor response or hypotension, as is characteristic with other ergot alkaloids.[76] In human subjects ergonovine produces practically no effects [13] or causes a slight increase in systolic and diastolic blood pressure with a slight slowing of the pulse, the effect being about half as great as that produced by ergotamine tartrate.[77]

In contrast, a fall in blood pressure is produced by ergonovine in anesthetized (ether, chloralose, evipal) cats [78] and etherized dogs.[66] Brown and Dale [67] believe that this depressor effect, which is accentuated by depressed respiration, is due to a depression of some vasomotor controlling center in the forebrain, the pressor effect being chiefly due to an action on spinal vasomotor centers rather than to peripheral effects. "The vasomotor effects of the alkaloid are the resultants of a complicated antagonism of actions at different levels." [67]

In contrast to the vasodilatation produced on perfusion of the hind limbs of the cat,[67] the leg vessels of the frog [68] and the ear vessels of the rabbit [66] are constricted by ergonovine.

The action on the heart itself appears to be unimportant in the production of the circulatory effects. Although decrease in the rate and amplitude of the frog heart on perfusion with ergonovine $1:10^6$ has been observed,[66] negative results have been reported from experiments on the isolated cat [66] and rabbit [67] heart.

In the rabbit, ergonovine inhibits the effect of stimulation of the depressor nerve but is only about one-half as strong in this regard as ergotamine.[71]

Uterine Action.—The high sensitivity of the human uterus to ergonovine emphasized in earlier reports [79] is in agreement with the results of animal experimentation in which uterine stimulation is the only specific effect produced by small doses of the alkaloid.

Ergonovine in very high dilutions ($1:2\times10^8$, [68] $1:3\times10^8$, $1:5\times10^8$, [7]) stimulates the isolated rabbit uterus to prompt and prolonged rhythmic contrac-

63. Smith, Sydney, and Timmis, Geoffrey Millward: The Alkaloids of Ergot: Part VIII, New Alkaloids of Ergot: Ergosine and Ergosinine, J. Chem. Soc., 1937, p. 394.

64. The Relationship of the Recently Discovered Ergot Alkaloids, Brit. M. J. **2**: 1114 (Dec. 7) 1935. Chen, K. K.; Swanson, E. E., and Hargreaves, C. C.: Ergometrinine, Proc. Soc. Exper. Biol. & Med. **34**: 183-185 (March) 1936. Raymond-Hamet: L'action physiologique de l'ergométrinine, est-elle supérieure, égale ou inférieure à celle de son isomère l'ergométrine? Compt. rend. Soc. de biol. **120**: 1208-1212 (Dec. 21) 1935. Stoll, Rothlin, Löller and Dale.[69]

65. Stoll, Arthur: Active Constituents of Ergot, Pharm. Monatschr. **18**: 146, 1937; footnotes 41 and 60.

66. Rothlin (footnotes 68 and 71).

67. Brown, G. L., and Dale, Sir Henry: The Pharmacology of Ergometrine, Proc. Roy. Soc., London s. B **118**: 446-477 (Oct. 3) 1935.

68. Rothlin, E.: Ueber ein neues Mutterkornalkaloid, Schweiz. med. Wchnschr. **65**: 947 (Sept. 28) 1935.

69. Brown and Dale.[67] Rothlin.[68]

70. Custer, R. P.: The Experimental Pathology of Ergotism, Am. J. M. Sc. **195**: 452-457 (April) 1938. Rothlin.[71] Brown and Dale.[67] Davis, Adair, Chen and Swanson.[66] Thompson.[5]

71. Rothlin, E.: Sur les propriétés pharmacologiques d'un nouvel alcaloide de l'ergot de seigle, l'ergobasine, Compt. rend. Soc. de biol. **119**: 1302-1304 (July 20) 1935.

72. Brown and Dale.[67] Davis, Adair, Chen and Swanson.[66] Rothlin, footnotes 68 and 71.

73. Thompson, footnotes 7 and 75.

74. Raymond-Hamet: Sur quelques effets pharmacologiques de l'ergométrine, nouvel alcaloide de l'ergot de seigle, Compt. rend. Acad. d. sc. **201**: 176-179 (July 8) 1935.

75. Thompson, Marvin, R.: A Comparison of the Pharmacological Syndromes of Ergosetrine (Ergonovine) and the Ergotoxine Group of Ergot Alkaloids, J. Am. Pharm. A. **26**: 803-816 (Sept.) 1937.

76. Brown and Dale.[67] Raymond-Hamet.[74]

77. Lennox, William G., and Leonhardt, Hildegarde C.: The Flow and Concentration of Blood as Influenced by Ergot Alkaloids and as Influencing Migraine, Ann. Int. Med. **11**: 663-670 (Oct.) 1937. Lennox, W. G.: Ergonovine versus Ergotamine as a Terminator of Migraine Headache, Am. J. M. Sc. **195**: 458-468 (April) 1938.

78. Rothlin.[71] Davis, Adair, Chen and Swanson.[66] Brown and Dale.[67] Thompson.[75]

79. Davis, Adair, Rogers, Kharasch and Legault.[9] Dudley and Moir.[10] Kharasch and Legault.[11]

tions [80] in contrast to the relative lack of sensitivity to ergotoxine.[81] Rothlin records the effect on the rabbit uterus in vitro [68] and in situ [82] as being twice as strong as that of ergotamine corresponding to their molecular weights and states that it is more easily washed out in vitro than ergotamine.[82] A much greater difference between the effective doses of these two alkaloids on the puerperal rabbit uterus in situ is indicated by other work.[83]

The isolated uterus of the virgin guinea pig is even more sensitive,[84] responding to dilutions of $1:10^7$,[85] $1:2\times10^7$,[48] or even to $1:10^8$.[67] However, this preparation shows equal sensitivity to ergotoxine, although the response to the former drug is slightly more abrupt.[67] In the guinea pig as in other animals the most striking effects are on the uterus in situ, within a few days after parturition, the response to intravenous injection being more prompt than with ergotoxine and stimulation of rhythm being the outstanding effect, whereas increases in tone predominate with the latter drug.[67]

Ergonovine increases the tone and activity of the nonpregnant cat uterus, virgin or parous, but in a manner indistinguishable from ergotoxine and ergotamine, as is also true in the early stages of pregnancy. However, the puerperal uterus shows striking sensitivity, ergonovine $1:75\times10^6$ initiating contractions continuing for hours in otherwise quiescent isolated preparations.[67] The uterus in situ behaves similarly,[67] responding to doses of from 0.05 to 0.1 mg. intramuscularly, while ergotamine usually produced no activity in doses up to 2 mg.[83]

A high degree of sensitivity has also been reported for the puerperal dog uterus in situ.[86]

Abortion has been produced in animals by ergonovine, but the results are too variable and few in number to justify a definite statement regarding the necessary dosage and probability of occurrence.[87]

Apparently the outstanding features of the action of ergonovine on animal uteri are manifested in the puerperal period when its prompt action and its effectiveness in small doses or high dilutions distinguish it from ergotoxine and ergotamine. The uterus in situ responds essentially by increased rhythmic contractions,[88] continuing for hours,[89] although an increase in tone is a prominent effect in the initial stages of the action.[90]

Sympathomimetic Action. — Ergonovine produces mydriasis on local application,[48] and mydriasis and exophthalmos in the general action of toxic doses in rabbits and cats in contrast to ergotoxine [67] and ergotamine,[91] the usual effect of which in the cat is myosis. A relaxation of the isolated intestine of the rabbit is produced, which may be prevented by ergotoxine [48] or ergotamine.[10] In contrast, the guinea pig's jejunum responds by a tonic contracture, which may also be annulled by ergotoxine,[67] and Thompson [75] reports relaxation followed by contraction of the isolated intestine of the guinea pig. Even the response of the isolated uterus of the rabbit is diminished by ergotoxine,[92] just as the latter drug abolishes the effect of epinephrine on this tissue. The blood sugar of the rabbit and dog is increased very little by ergonovine, but it increases the action of epinephrine in this regard.[93] Such observations indicate a peripheral sympathomimetic action, although, as already mentioned,[67] the manifestations of sympathetic stimulation in the intact animal may be due principally to a central effect.

Epinephrine Inhibiting Action.—Neither the general pressor response of epinephrine [94] nor its vasoconstricting effect in the kidney and intestine in situ,[68] in the Laewen-Trendelenburg frog perfusion [48] and in the perfusion of the hind limbs of the cat,[67] is prevented by ergonovine as it is by ergotoxine and ergotamine. The same failure of ergonovine to inhibit the action of epinephrine has been demonstrated on the rabbit uterus [95] and the seminal vesicle of the guinea pig.[96] However, it may not be entirely devoid of this action, as it has been observed to some degree on the circulatory system [97] and uterus [98] after very large and repeated doses. Even when such action does appear on in vitro preparations it may be removed by a change in solution, which is not possible with ergotoxine.[67]

Additional Actions.—Large doses of ergonovine produce an increase in rate but a decrease in the volume of respiration in cats and rabbits,[68] the respiratory center of the cat being more strongly affected than with ergotamine.[91] Toxic amounts lower the temperature of the mouse [68] and increase that of the cat and rabbit,[99] the latter effect being greater than that with ergotamine.[91] Ergonovine, in doses not producing side actions, produces diuresis in dogs in contrast to the antidiuretic action of ergotoxine and ergotamine.[100] This action is not observed clinically.[13] In vitro it inhibits the splitting of acetylcholine by choline esterase.[101]

Occurrence and Assay.—It was recognized early in the investigation of ergonovine that it did not occur in constant amounts in all specimens of ergot, and in certain samples (e. g. Russian ergot in contrast to Spanish and Portuguese ergots) it was entirely lacking.[102] Even ergots obtained from one locality may vary in this regard.[103] The results of various workers indicate a content of from 0.05 to 0.2 mg. per gram

80. Rothlin.[75] Brown and Dale.[67] Davis, Adair, Chen and Swanson.[48] Thompson.[7]

81. Thompson.[7] Davis, Adair, Chen and Swanson.[48] Brown and Dale.[67]

82. Rothlin, E.: Neues zum Mutterkornproblem, Arch. f. exper. Path. u. Pharmakol. **181**: 134-155, 1936.

83. Oettel, H., and Bachmann, H.: Untersuchungen am puerperalen Säugeruterus über Hypophysin, Ergometrin und Mutterkornextrakte, Arch. f. exper. Path. u. Pharmakol. **185**: 242-258, 1937.

84. Thompson.[7] Davis, Adair, Chen and Swanson.[48] Brown and Dale.[67] Küssner and Sieckmann.[68] Thompson.[75]

85. Küssner, W., and Sieckmann, W.: Ergometrin, ein neues Mutterkornalkaloid, München. med. Wchnschr. **85**: 725-726 (May 1) 1936.

86. Davis, Adair, Chen and Swanson.[48] Swanson, Hargreaves and Chen.[107] Azuma, Kumagai and Usui.[88] Küssner and Sieckmann.[68]

87. Reisel, J. H.: Ergot Preparations, Acta brev. Neerland. **7**: 81-82, 1937; Chem. Abstr. **31**: 6329, 1937. Thompson.[4] Brown and Dale.[67] Rothlin.[68]

88. Azuma, A.; Kumagai, H., and Usui, T.: Effect of New Alkaloid Ergometrine (Ergonovine) on Chronic Uterine Fistula in Unanesthetized Dog, Jap. J. M. Sc. IV. Pharmacol. **9**: 205-206, 1936. Brown and Dale.[67] Küssner and Sieckmann.[68]

89. Brown and Dale.[67] Küssner and Sieckmann.[68]

90. Oettel and Bachmann.[83] Davis, Adair, Chen and Swanson.[48] Küssner and Sieckmann.[68]

91. Rothlin, footnotes 68 and 82.

92. Swanson, Hargreaves and Chen.[107] Thompson, footnotes 7 and 75.

93. Rothlin, E.: Pharmacologische Grundlagen der Mutterkorntherapie, München. med. Wchnschr. **84**: 321-322 (Feb. 26) 1937; footnotes 68 and 71.

94. Rothlin, footnotes 68 and 71. Davis, Adair, Chen and Swanson.[48] Brown and Dale.[67] Thompson, footnotes 7, 26 and 75. Raymond-Hamet.[74]

95. Rothlin, footnotes 68 and 71. Davis, Adair, Chen and Swanson.[48] Küssner and Sieckmann.[68] Chen, Swanson, Kleiderer and Clowes.[26]

96. Brown and Dale.[67] Rothlin.[68]

97. Davis, Adair, Chen and Swanson.[48] Brown and Dale.[67] Raymond-Hamet.[74] Rothlin.[68]

98. Thompson, footnotes 7 and 75. Brown and Dale.[67]

99. Rothlin, footnotes 68 and 82. Brown and Dale.[67]

100. Zunz, Edgard, and Vesselovsky, Olga: Action de l'ergométrine et de l'ergobasine sur la diurèse, Compt. rend. Soc. de biol. **120**: 1360-1362 (Nov. 20) 1935; **120**: 270-272 (No. 25) 1937.

101. Navratil, Ernst: Ueber die Beeinflussung der Cholinesterase durch Ergobasine, Klin. Wchnschr. **16**: 64-65 (Jan. 9) 1937.

102. Kharasch and Legault.[11] Stoll, Rothlin, Löffler and Dale.[10] Stoll.[18]

103. Davis, M. Edward: The Use and Abuse of Ergot and Pituitary, J. A. M. A. **109**: 1631-1635 (Nov. 13) 1937.

of ergot in samples which contain it.[104] Of course, a part of this variation may be due to the efficiency of isolation and to the purity of the final product. In any case it is present in much smaller concentrations than the ergotoxine-ergotamine group, which may reach 2 mg. per gram [105] and according to U. S. P. requirements must be 0.5 mg. per gram.

Owing to such variations in occurrence and to the marked activity of ergonovine on the uterus in comparison with that of other ergot alkaloids, the problem of assay is of great importance and has been considered in numerous publications.[106] The assay of pure preparations of ergonovine uncontaminated by other alkaloids of ergot is a comparatively simple problem, a variety of tests being applicable.[107] However, in crude preparations containing such other alkaloids as ergotoxine and ergotamine it becomes more difficult, since the latter produce comparable results in the colorimetric and cock's comb methods. Consequently such assays would be a measure neither of the content of any particular alkaloid nor of the clinical potency of the preparation. Although ergonovine has a much stronger effect than the other alkaloids on the isolated rabbit uterus, even by this method the presence of the latter substances and also of amines in galenic preparations would be complicating factors. This is especially true, if, as already stated, the response of the isolated rabbit uterus to ergonovine is diminished by ergotoxine.[108] It would appear that a separation of ergonovine from the other group of alkaloids would be necessary before assay, unless such assays were made clinically on the postpartum human uterus. Assays by the colorimetric method [109] and on the puerperal cat or rabbit uterus in situ [62] involving a previous separation have already been proposed. Naturally the usefulness of such methods must be learned by further experience with them. Of course, a simpler solution of the problem from the therapeutic point of view would be the use of pure alkaloids rather than of galenic preparations. Such a practice would also be desirable with regard to the production of the specific effects of the individual alkaloids.[10]

CLINICAL INVESTIGATIONS

Effective Dosages and Character of Action.—It was early observed that the postpartum uterus is extremely sensitive to ergonovine. Effective dosages originally cited by Dudley and Moir [16] were from 0.5 to 1 mg. orally, from 0.25 to 0.5 mg. intramuscularly and from 0.05 to 0.1 mg. intravenously. Positive effects have been produced with less than 0.05 mg. intravenously, although 0.2 mg. has been described as an optimal intravenous dose and 0.4 mg. is considered suitable for administration by mouth, sublingually or intramuscularly.[15] Typical responses may be obtained, however, from 0.2 mg. by mouth.[21] Doses of approximately this range have proved effective in other investigations [110] and have been safely increased to 1.5 mg. by mouth and 0.75 mg. intramuscularly.[111]

The rapidity of response has proved to be a distinctive feature in contrast to the prolonged latent period characteristic of the other alkaloids. The time elapsing between administration and effect is approximately from six to eight minutes, from three to four minutes and from one to two minutes or less after administration by mouth, intramuscularly and intravenously respectively. On the contrary, ergotoxine and ergotamine, in doses by mouth as high as 3 mg. or more, which produce unpleasant side effects, may cause no action on the uterus or the action may appear only after a latent period of from one half to three quarters of an hour or longer.[112] Even on injection, twenty minutes may elapse before the onset of action.[111]

The character of the response has also been described in detail in these studies. On the quiescent postpartum uterus an intravenous injection results in an abrupt increase in tone developing over the course of about fifteen seconds. This is followed by slight and increasing contractions with some fall toward normal in tone, the record henceforth resembling that following administration by other routes.[15] In the latter cases the development in tone is less rapid, with slight contractions which gradually become less frequent. The early phase of the action, lasting for from forty-five to ninety minutes, has been described as a tonicoclonic stage in which a tonic contraction is the predominant feature.[113] The early spasm is considered to be due to contractions following each other in such close succession that the uterus does not have time to relax.[50] With a gradual decrease in tone accompanied by a greater prominence of rhythmic contractions this phase gradually changes into one lasting up to three hours or longer characterized by successive rhythmic contractions with complete relaxation intervening, the contractions becoming less frequent and weaker as the effect subsides. The tonic element of the action is apparently less marked than that resulting from ergotoxine and ergotamine,[111] the tonus increase being proportionately small in relation to the rhythmic contractions produced.[114]

Duration of Action.—The early assumption [115] that the action of ergonovine on the uterus is abrupt and transient in comparison with a more persistent effect produced by ergotoxine and ergotamine might well have been inferred, owing to its high water solubility and consequent easier removal from its site of action, as indeed has been observed in in vitro experiments.[62] However, in both animal [99] and clinical [116] investigations it has been demonstrated that the action persists for from three to four hours or longer. Rothlin,[117] Stoll,[99] Heyrowsky [118] and Wirth [119] consider this duration of action to be overestimated on account of the possible contamination with ergotoxine and ergotamine

104. Dudley and Moir.[16] Dudley.[17] Stoll and Burckhardt.[18] Stoll.[43] Rothlin.[106] Thompson.[7]

105. Rothlin, E.: Ueber die Standardisierung von Mutterkorn, Arch. f. Exper. Path. u. Pharmakol. **184**: 69, 1936.

106. Thompson,[7] Swanson, Hargreaves and Chen.[107] Hampshire and Page.[20] Rothlin.[105] Oettiel and Bachmann.[62]

107. Swanson, Edward E.; Hargreaves, Chester C., and Chen, K. K.: The Question of Assaying Ergotocine, the New Ergot Principle, J. Am. Pharm. A. **24**: 835-839, 1935.

108. Thompson, footnotes 7 and 75. Swanson, Hargreaves and Chen.[107]

109. Trabucchi, Emilio: The Determination of Ergonovine in Ergot Preparations, Boll. Soc. ital. biol. sper. **12**: 232-234 (June) 1937. Glycart, C. K.: Report on the Chemical Assay for Ergot Alkaloids, J. A. Official Agric. Chemists **20**: 566-568, 1937. Hampshire and Page.[20]

110. Kharasch and Legault.[21] Davis.[100] Hauck and Möller-Christensen,[112] Moir, footnotes 50 and 111.

111. Moir, Chassar: The Merits and Demerits of Oxytocic Drugs in the Postpartum Period, Proc. Roy. Soc. Med. **28**: 1654 (2) 1935; Use of Oxytocic Drugs Postpartum, Brit. M. J. **2**: 178-179 (July 27) 1935.

112. Adair, Davis, Kharasch and Legault.[15] Moir.[111]

113. Hauck, E., and Möller-Christensen, E.: Preliminary Results with Ergonovine, Acta obst. et gynec. Scandinav. **16**: 152-159, 1936; New Ergot Preparations—Ergometrine, J. Obst. & Gynaec. Brit. Emp. **43**: 1145-1151 (Dec.) 1936.

114. Runge, H.: Ueber Erfahrungen mit Ergometrin, Zentralbl. f. Gynäk. **60**: 1986-1990 (Aug. 22) 1936.

115. Burn, J. H.: The Isolation of Ergometrine, Pharmaceut. J. **134**: 357 (March 30) 1935. Stoll, Rothlin, Löller and Dale.[99]

116. Adair, Davis, Kharasch and Legault.[15] Stoll.[43] Hauck and Möller-Christensen.[112] Moir, footnotes 50 and 111. Antoine.[108]

117. Rothlin, E.: The Present Status of the Ergot Problem, M. Rec. **148**: 449-452 (June 2) 1937; footnote 93.

118. Heyrowsky, K.: Neo-Gynergen, ein Präparat aus reinen Mutterkornalkaloiden, Zentralbl. f. Gynäk. **61**: 42-46 (Jan. 2) 1937.

119. Wirth, L.: Klinische Erfahrungen mit einem neuen Mutterkornwirkstoff, München. med. Wchnschr. **84**: 324 (Feb. 26) 1937.

of the ergonovine preparations used and on account of the previous administration of ergotoxine or ergotamine in certain clinical experiments which might account for the prolonged action observed. However, it is doubtful whether such criticisms could apply in many instances. Although the action may persist as stated, the duration of the spasm may be only half that of the ergotamine-ergotoxine group and the total duration of the effect probably less than that of these alkaloids.[120]

Side Actions.—A favorable aspect in the clinical use of ergonovine is the rarity of undesirable side actions, which frequently occur with the other alkaloids,[121] and posterior pituitary extract.[122] In one series of more than 200 cases in which 0.25 or 0.5 mg. of ergonovine was administered orally, no side actions were observed.[114] However, in a few cases nausea and vomiting has been encountered,[15] and Moir [123] reports three instances of unusual reactions.

THERAPEUTIC USES

Before the onset of labor the uterus is apparently somewhat insensitive to the action of ergonovine,[50] although some effect has been reported.[124] It gave inconclusive results when it was tried in a few cases for the induction of labor [15] and for the interruption of a four to five months pregnancy.[114] Also in cesarean section the uterus does not respond to ergonovine before removal of the fetus unless labor has already commenced.[50]

Its administration in labor before the birth of the child is considered unsafe [125] although it has been used in a few selected cases of uterine inertia in the second stage of labor with successful results.[114]

Ergonovine probably finds its most extensive application in the treatment of postpartum hemorrhage, having been successfully used in several series of cases.[126] It is probably more reliable for this purpose than posterior pituitary extract.[127]

If necessary it may be safely used in the third stage of labor in doses of approximately 0.25 mg. by injection or by mouth, as indicated by several investigations involving this procedure.[128] The usual but not invariable result has been rapid placental separation and expulsion with minimal bleeding. Moir [111] favors its use in cases of third stage hemorrhage or on failure of simple methods to produce placental expulsion but not as a routine procedure.

The final answer regarding the use of ergonovine in the puerperium has not been reached, although there have been several controlled studies in this regard. Davis, Adair and Pearl [21] and Wirth [119] report favorably concerning its action in reducing foul lochia, lochial obstruction, subinvolution and morbidity. Der Brucke [129] and Tuck [130] (ergoklonin) also consider it to be of benefit. On the contrary, Moir [131] reached the tentative conclusion that its routine use in the puerperium offered no advantages and considered it contraindicated in the presence of uterine sepsis.

Uniformly satisfactory results are reported for its use in cesarean section with respect to prompt separation of the placenta and the control of hemorrhage. It has been injected as the baby was delivered,[15] before incision of the uterus,[50] and directly into the uterine wall after extraction of the baby.[119]

It would appear that ergonovine is worthy of further trial in the treatment of incomplete abortion.[132] Although not all reports are favorable regarding the expulsion of retained secundines, it is undoubtedly of value in the control of bleeding.

After diagnosis it may be of value as a palliative and temporary measure in certain cases of menorrhagia and metrorrhagia until the underlying pathologic condition can be corrected.[133]

Positive results have been reported for the relief of migraine headache by ergonovine, although it was effective in a much lower percentage of cases than was ergotamine.[77]

Importance of Ergonovine.—The isolation and clinical trial of ergonovine has prompted the expression of various opinions regarding its importance in the realm of ergot therapy. Dale [134] and Dudley and Moir [16] consider it of greater therapeutic importance than all the hitherto known alkaloids of ergot and believe that it forms the basis for ergot therapy at least as far as the uterine action is concerned. It is suggested that the presence of the other alkaloids may actually have a deleterious effect. Moir [50] expresses the belief that it should be used wherever there are indications for ergot therapy and that it completely supplants the older preparations.

Adair [15] hails it with similar enthusiasm, considering it the active principle which is responsible for most if not all of the desirable oxytocic effect of ergot. Runge [114] and Küssner [135] also seem to agree that it is of prime importance in ergot therapy. Stoll [136] considers such opinions too sanguine: Owing to the small amounts of ergonovine in many ergots, the traditional action of the crude drug may not be wholly explained by its presence. Also in the light of its presumably short duration of action it plays only a limited role in ergot therapy and should be supplemented by a drug with a more persistent action when this is desired. Furthermore, it has been pointed out by Rothlin and Löffler [10] that it at least cannot replace ergotoxine and ergotamine in the treatment of those conditions in which the inhibiting effect on the sympathetic nervous system is indicated. The wide therapeutic use which already exists will undoubtedly settle such differences of opinion in the near future.[137]

120. Moir, footnotes 50 and 111. Antoine.[124]
121. Davis, Adair, Rogers, Kharasch and Legault.[9] Dudley and Moir.[16]
122. Adair, Davis, Kharasch and Legault.[15] Davis.[102] Moir.[111]
123. Moir, Chassar: Ergometrine: The Possibility of Idiosyncrasy, Brit. M. J. 2: 1028 (Nov. 21) 1936.
124. Antoine, Tassilo: Die klinische Verwendbarkeit der neuen Secale-Alkaloides Ergobasin, Wien. klin. Wchnschr. 50: 999-1001 (July 2) 1937.
125. Moir.[50] Runge.[114]
126. Moir.[50] Adair, Davis, Kharasch and Legault.[15] Davis, Adair and Pearl.[21] Hauck and Möller-Christensen.[118] Wirth.[119] Runge.[114]
127. Moir.[50] Adair, Davis, Kharasch and Legault.[15] Wirth.[119]
128. Tritsch, J. E., and Behm, K. H.: Clinical Experience with a New Ergot Alkaloid, Am. J. Obst. & Gynec. 34: 676-679 (Oct.) 1937. Adair, Davis, Kharasch and Legault.[15] Moir.[111] Runge.[114] Tuck.[130]
129. DerBrucke, M. G.: Notes on the Use of the Recently Introduced Ergot Alkaloids in the Puerperium, Am. J. Obst. & Gynec. 32: 474-478 (Sept.) 1936.
130. Tuck, Vernon L.: A Clinical Test of the Newly Recognized Oxytocic Principle of Ergot and a New Method of Administration, Am. J. Obst. & Gynec. 30: 718-723 (Nov.) 1935.
131. Moir, footnotes 50 and 111.
132. Davis, Adair and Pearl.[21] Moir.[50] Runge.[114] Wirth.[119]
133. Davis, Adair and Pearl.[21] Davis.[102] Moir.[50] Runge.[114]
134. Dale, Sir Henry: Die Pharmakologie des Mutterkorns, Schweiz. med. Wchnschr. 65: 885 (Sept. 14) 1935. Stoll, Rothlin, Löffler and Dale.[10]
135. Küssner, W.: Recent Results in Ergot Research, Angew. Chem. 50: 34-38, 1937.
136. Stoll, Rothlin, Löffler and Dale.[10] Stoll, footnotes 41 and 60.
137. Reviews not directly referred to in the text:
Barger, George: The Alkaloids of Ergot, Analyst 62: 340-354 (May) 1937.
Tanret, G.: Recent Discoveries in the Chemistry of Ergot, 1930-1935, J. Pharm. Chim. 24: 269-283, 1936.
Nelson, Erwin E., and Calvery, Herbert O.: Present Status of the Ergot Question, Physiol. Rev. 18: 297-327 (April) 1938.

SUMMARY

Ergonovine, an alkaloid of ergot, was isolated independently and by contemporaneous work in four laboratories.

It crystallizes readily and forms a variety of crystalline salts; characteristic physical properties have been described for both the base and the salts.

In contrast to other alkaloids of ergot, ergonovine is appreciably soluble in water and comparatively insoluble in chloroform; its salts are markedly soluble in water.

It is less readily precipitated by Mayer's reagent than other ergot alkaloids but gives the characteristic color reactions of this group. The color developed with *p*-dimethylaminobenzaldehyde is quantitatively greater than with the other alkaloids, in keeping with the smaller molecule of ergonovine.

Ergonovine, $C_{19}H_{23}O_2N_3$, consists of a combination of lysergic acid, common to all ergot alkaloids, and *d* 2-amino propanol-1.

In the intact animal and in human subjects the only appreciable effect of moderate doses is on the uterus, which is especially sensitive in the puerperal state. It is effective in smaller doses and concentrations than are other ergot alkaloids, such doses being remarkably free from unpleasant side actions. It is further characterized by its prompt action even when administered by mouth. It increases both the tone and the rate and amplitude of rhythmic contractions of the uterus, the latter effect probably being proportionately greater than the tonus changes. The duration of the effect, although probably less than that of ergotoxine and ergotamine, is at least comparable with that of the latter alkaloids.

It is less toxic than ergotoxine and ergotamine but in poisonous doses produces effects similar to those of the latter alkaloids. Although ergonovine produces the characteristic cock's comb reaction, it shows definitely less tendency to produce gangrene than ergotoxine and ergotamine.

The circulatory effects, which are referable to actions on the central nervous system and peripheral vascular mechanism rather than to cardiac effects, vary with the animal and with experimental conditions.

Ergonovine shows a definite sympathomimetic effect and little or no inhibition of epinephrine action.

It may be assayed by a variety of procedures when in the pure form but at present cannot be quantitatively determined in the presence of other alkaloids of ergot. Suggested methods involve a separation of ergonovine from the ergotoxine-ergotamine group before assay.

Its greatest clinical value appears to be in the treatment of postpartum hemorrhage, being safely administered at the beginning of the third stage if necessary. Likewise it has been of value in the control of hemorrhage following cesarean section. Many investigators favor its use in the puerperal period for the promotion of involution and the prevention and control of sepsis, but this use is not universally accepted. Variant results have also been obtained in the treatment of incomplete and inevitable abortion. It may be used as a palliative measure in certain cases of menorrhagia and metrorrhagia.

Many authorities believe that ergonovine forms the basis for all ergot therapy involving uterine action and that it is responsible for the traditional effect of ergot, while others are less enthusiastic concerning its value.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

MRS. PALEY'S BABY FOOD—STRAINED APPLES

Manufacturer.—Paley-Sachs Food Company, Houston, Texas.

Description.—Canned cooked sieved apples, containing a small amount of added dextrose.

Manufacture.—Colorado Jonathan apples are thoroughly washed, trimmed, inspected, cooked in air-tight steam pressure cookers for five minutes with added dextrose, sieved, filled into glass jars and heat processed.

Analysis (submitted by manufacturer).—Moisture 77.4%, total solids 22.6%, ash 0.3%, fat (ether extract) 0.1%, protein (N × 6.25) 0.2%, reducing sugars as dextrose 15.7%, sucrose 1.7%, crude fiber 0.8%, total carbohydrates other than crude fiber (by difference) 21.2%, calcium (Ca) 0.006%, phosphorus (P) 0.02%, iron (Fe) 0.0008%.

Calories.—0.9 per gram; 25.6 per ounce.

CLAPP'S PUREE OF GREEN BEANS

Manufacturer.—Harold H. Clapp, Incorporated, Rochester, N. Y.

Description.—Canned sieved green beans, seasoned with salt.

Manufacture.—Fresh green beans, grown under contract with the manufacturer, are cleaned, sorted, washed, again sorted, and precooked under pressure in an atmosphere of steam. Salt is added and the partially cooked beans are sieved in an atmosphere of steam, vacuum treated to attain the desired consistency, automatically filled into cans, and heat processed.

Analysis (submitted by manufacturer).—Moisture 91.5%, total solids 8.5%, ash 0.8%, fat (ether extract) 0.2%, protein (N × 6.25) 1.6%, crude fiber 0.9%, carbohydrates other than crude fiber (by difference) 5.0%.

Calories.—0.3 per gram; 8 per ounce.

CELLU BRAND ORANGE JUICE

Distributor.—Chicago Dietetic Supply House, Inc., Chicago.

Description.—Canned California Valencia orange juice.

Manufacture.—Manufactured in essentially the same manner as Treesweet Pure California Orange Juice (THE JOURNAL, June 15, 1935, p. 2187).

Analysis (submitted by manufacturer).—Moisture 85.9%, total solids 14.1%, ash 0.4%, fat (ether extract) 0.1%, protein (N × 6.25) 1.1%, reducing sugar as invert 5.6%, sucrose (by copper reduction) 4.8%, crude fiber 0.02%, carbohydrates other than crude fiber (by difference) 11.5%, titratable acidity as citric acid 1.0.

Calories.—0.51 per gram; 14 per ounce.

MRS. PALEY'S BABY FOOD—STRAINED EVAPORATED PEARS

Manufacturer.—Paley-Sachs Food Company, Houston, Texas.

Description.—Cooked, sieved, sulfured dried pears, packed with added dextrose.

Manufacture.—Dried sulfured pears are washed, soaked, pressure cooked with added dextrose, strained, filled into glass jars, vacuum sealed and heat processed. A small amount of lemon juice is added for flavor.

Analysis (submitted by manufacturer).—Moisture 72.4%, total solids 27.6%, ash 0.5%, fat (ether extract) 0.1%, protein (N × 6.25) 0.6%, crude fiber, 1.4%, reducing sugars as dextrose 13.2%, sucrose 2.2%, total carbohydrate other than crude fiber (by difference) 25.0%, iron (Fe) 0.0011%, phosphorus (P) 0.025%, calcium (Ca) 0.021%, sulfur dioxide (SO_2) 0.033%.

Calories.—1 per gram; 28.4 per ounce.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street - - - Chicago, Ill.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - - Seven dollars per annum in advance

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SATURDAY, DECEMBER 10, 1938

GAS GANGRENE

All recent reports on gas gangrene in man agree essentially on the increase of this condition in civil life. Following injuries sustained in the World War gas gangrene was common. Today the condition is becoming more important because of the more frequent occurrence of crushing wounds and lacerations following traffic and industrial accidents. While its frequency is difficult to determine accurately, the increasing reports in the literature seem to offer sufficient evidence of its widespread nature.

A recent review [1] of the morbidity and mortality due to gas gangrene in New York State exclusive of New York City, while admittedly incomplete, reports 208 hospitalized cases between 1932 and 1936. These cases are placed in four groups: those presenting records positive for gas gangrene clinically and bacteriologically, those presenting records incomplete but with sufficient evidence to be included as gas gangrene, those presenting records that made the diagnosis questionable and those in which the data were too incomplete for an accurate diagnosis. With the omission of the last two groups 135 cases were recorded, ninety-one of them resulting from trauma, thirteen from clean amputations, seven from pregnancy, five from gunshot wounds and nineteen from miscellaneous causes. When compared with the incidence of tetanus, infection by this group of spore-bearing bacteria is probably as frequent. According to White,[2] gas infection usually occurs in four types of wounds: crushing injuries in which the skin is torn, puncture wounds with a great deal of hemorrhage, particularly if a foreign body has been implanted, extensive lacerations of tissues with gross soiling with dirt, and badly soiled compound fractures. Ramsay [3] states that gunshot wounds and compound fractures offer the most favorable environmental conditions for the development of Clostridium welchii or other spore-bearing anaerobes, since damaged muscle tissue is the perfect medium for the growth and development of these organisms. Less commonly, gas gangrene has been reported following abortion [4] and as a result of hypodermic injection.[5] Organisms of this group, including Clostridium welchii, Vibrion septique and Clostridium oedematiens, are so widely distributed in nature that little can be done to eradicate the source of infection.

The best treatment for gas gangrene is prophylactic. Penfold and Tolhurst [6] have reported promising attempts at the immunization of animals and man with alum-precipitated formol toxoid made from Clostridium welchii toxin. After preliminary work on experimental animals volunteers were treated with the toxoid and the level of antitoxin was measured at various intervals thereafter. The evidence presented, they believe, suggests that this toxoid is suitable material for immunizing man against gas gangrene due to Clostridium welchii, although the level of antitoxin necessary for protection has not as yet been determined. Auspicious as this work may be, it is not likely that the frequency of gas gangrene in peace time is such that mass immunization is likely to be a practical preventive measure in the near future.

The prophylactic treatment of patients who have extensive lacerations or other injuries which are recognized as predisposing to gas gangrene has been carefully outlined in a number of the recent discussions. Lower and Tormey [7] state that in carrying out a débridement properly it is important that adequate exposure of the depths of the wound be obtained. The wounds in which dead spaces or pockets are apt to occur are best cared for by placing Dakin tubes in their depths through which irrigation may be carried out every two hours. They also recommend the use of a prophylactic dose of polyvalent gas bacillus antitoxin (and tetanus antitoxin) to every patient with extensive or suspicious wounds. Although Malone [8] believes that a larger dose of Clostridium welchii antitoxin is to be preferred to the polyvalent antitoxin usually supplied, the majority seem to agree that the polyvalent antitoxin in suitable quantities is satisfactory.

In spite of suitable precautionary measures there are some instances in which gas gangrene develops, and treatment therefore becomes of paramount importance. Surgical exploration with the introduction of air and probably diluted solution of sodium hypochlorite should

1. Mitchell, O. W. H.; Bryant, T. L., and Chapman, O. D.: Gas Gangrene: Morbidity and Mortality in New York State (Exclusive of New York City)—Based on General Hospital Reports for the Years 1932-1936 Inclusive, New York State J. Med. **38**: 1022 (July 15) 1938.
2. White, R. J.: Gas Gangrene, Texas State J. Med. **34**: 271 (Aug.) 1938.
3. Ramsay, C. H.: Gas Gangrene Infections in Industrial Practice with Especial Reference to Infections Following Compound Fractures and Other Accidents, South. M. J. **31**: 773 (July) 1938.
4. Dawbarn, R. Y., and Williams, Bryan: Three Cases of Cl. Welchii Infection Following Abortion, Brit. M. J. **2**: 279 (Aug. 6) 1938.
5. Jungmichel, G.; Kirschner, M., and Hahs, H.: Ueber die Gasbrandinfektion nach Injektion, München. med. Wchnschr. **85**: 125 (Jan. 28) 1938. Bittrolff, R.: Ueber Gasbrandinfektion nach Injektion, ibid. **85**: 590 (April 22) 1938.
6. Penfold, W. J., and Tolhurst, Jean C.: Formol-Toxoids in the Prophylaxis of Gas Gangrene, M. J. Australia **1**: 982 (June 26) 1937; Prophylaxis of Gas Gangrene in Man, ibid. **1**: 604 (April 2) 1938.
7. Lower, W. E., and Tormey, T. W., Jr.: Gas Gangrene and Its Treatment, S. Clin. North America **17**: 1385 (Oct.) 1937.
8. Malone, Battle: Gas Gangrene—Its Prevention and Treatment, J. Tennessee State M. A. **30**: 402 (Oct.) 1937.

in this event be employed at once. The use of antitoxin in large quantities intramuscularly or intravenously or in some cases around the infected area is also a procedure to be employed promptly.

The use of x-rays has been reported favorably,[9] and in the past few months several reports on the favorable effect of sulfanilamide or its derivatives in gas gangrene have appeared.[10] The effectiveness of prophylactic measures and improvement and addition of therapeutic technics for dealing with this disease should do much to minimize its dangers.

ANTIGENIC STRUCTURE OF SPERMATOZOA

The recent demonstration of a head-specific and a tail-specific antigenic fraction in mammalian spermatozoa, with a third or species-specific antigen common to the heads and the tails, is of basic biologic and immunochemical interest. Separation of spermatozoa into head and tail fractions was attempted forty years ago by Miescher.[1] He found that if fish spermatozoa are suspended in distilled water the relatively heavy heads can be broken off by carefully graduated centrifugation. Mammalian spermatozoa, however, cannot be broken up by this technic. Henle and his colleagues [2] of the Johnson Foundation for Medical Physics, University of Pennsylvania, have recently attempted such fragmentation by the modern technic of supersonic vibration. They found that bull, dog or rabbit spermatozoa were fairly completely broken up into head and tail fractions by exposure for seven minutes to vibrations of 9,000 cycles per second. Guinea pig spermatozoa required fifteen minutes and human spermatozoa twenty minutes for similar fragmentation. Final separation of the head and tail fragments was effected by fractional centrifugation. By repeated washings, head and tail suspensions can often be obtained 99 per cent pure. This degree of purity was confirmed by the use of a blood counting chamber and by a study of stained smears. Cleavage occurred uniformly at the junction of the midpiece and head except with human spermatozoa. With human cells a small part of the midpiece often remained with the head. No difference was noted in the microscopic appearance of the heads after separation, except with guinea pig spermatozoa, which often lost their acrosome.

The Pennsylvania investigators immunized rabbits against the head and tail fractions and against the intact spermatozoa of four different animal species. Tests of antigenic specificity were made by the complement fixation technic with confirmatory tests by slide agglutination. As shown by other investigators, cross reactions were obtained with the intact spermatozoa of different animal species. Cross reactions were obtained also with the head and tail fractions of the same animal species. By proper absorption of the antiserums, however, highly specific fractional antibodies were demonstrated. Thermolabile tail-specific and head-specific antigen fractions were thus recognized, as well as a coctostable heterophile or nonspecific fraction common to heads and tails. A fourth, nuclear-specific, fraction is suspected, not demonstrable in intact spermatozoa but readily demonstrable in the broken-off heads. Antibodies against this hypothetical nuclear-specific antigen are not formed on injection of intact spermatozoa but are formed when vibrated heads are injected. Whether or not the suspected nuclear antigen is a protein or a lipoid has not yet been determined.

The results obtained by the complement deviation technic were confirmed by a study of slide agglutination. Two types of agglutination were noted. The first was a head-specific agglutination or clumping of the heads, with the formation of a rosette of moving tails. The second was a tail-specific agglutination with adhesion or clumping of the tips of the tails. The latter resulted in a rosette of moving heads. Combined head and tail agglutination was obtained with native antiserums against intact spermatozoa, with a resulting netlike entanglement of whole cells.

Immunologists of the future may conceivably regard Henle's work as of basic historical interest, the first successful attempt at a serologic dissection of mammalian tissue cells. There seems no reason why some modification of his technic cannot be applied to other mammalian tissues.

NEW JERSEY MOSQUITOES AS POTENTIAL CARRIERS OF YELLOW FEVER

The demonstration by Bennett and his colleagues [1] of the Harvard Medical School that the common New Jersey mosquito is capable of transmitting yellow fever to monkeys seems to throw doubt on the conventional assumptions for other insect-borne diseases. Following experimental proof by Reed, Carroll and their co-workers in 1900-1901 that the subtropical mosquito variously known as Aedes aegypti, Stegomyia fasciata or Aedes argentens is capable of transmitting yellow fever to man, it was quite generally assumed by hygienists that this is the only species of mosquito capable of transmitting this infection. It was alleged in support of this assumption that the geographic distributions of Aedes aegypti and yellow fever are the same. Not till a quarter of a century later, after Stokes, Bower and

9. Kelly, J. F., and Dowell, D. A.: Present Status of the X-Rays as an Aid in the Treatment of Gas Gangrene, J. A. M. A. **107**: 1114 (Oct. 1) 1936.

10. Bohlman, H. R.: Gas Gangrene Treated with Sulfanilamide: Report of Three Cases, J. A. M. A. **109**: 254 (July 24) 1937. Natvig, H.: Eksperimentelle undersøkelser over virkningen av prontosil ved gasødeminfeksjoner, Norsk mag. f. lægevidensk. **99**: 631 (June) 1938. Fuller, G. W., and Kellum, J. M.: Prontosil and Sulfanilamide in the Treatment of Gas Gangrene, South. Surg. **7**: 305 (Aug.) 1938.

1. Miescher, Fritz: Arch. f. exper. Path. u. Pharmakol. **37**: 100, 1896.

2. Henle, Werner; Henle, Gertrude, and Chambers, L. A.: J. Exper. Med. **68**: 333 (Sept.) 1938.

1. Bennett, Byron L.; Baker, Fred C., and Sellards, Andrew Watson: Science **88**: 410 (Oct. 28) 1938.

Hudson (1928) had shown that rhesus monkeys are susceptible to yellow fever, was it practicable to make adequate tests of other species. Two other subtropical species of mosquitoes were then shown to be equally efficient vectors of yellow fever, while a third subtropical species would occasionally transmit the disease in an attenuated form.

The question was raised as early as 1904 by J. B. Smith [2] of Trenton, N. J., whether or not the disease could be transmitted by the common northern mosquito. An attempt was not made to answer this question, however, until 1935, when Baker established a colony of Aedes triseriatus in his local insectary at Cornell University and sent specimens to the Harvard Medical School for transmission tests. The species bred by Baker is common from Maine to Florida and has been identified as far west as Montana.

At the Harvard Medical School thirty-five of these northern mosquitoes were allowed to feed on a monkey dying from yellow fever. After this feeding the mosquitoes were kept for seventeen days at a temperature of 28 C. (82.4 F.) and six of the seven survivors then allowed to bite a healthy monkey. After an incubation period of six days this monkey showed a transient febrile reaction° (104 F.) lasting about twenty-four hours, after which it was without demonstrable symptoms for nearly a month. The monkey, however, died on the thirty-sixth day. Necropsy showed typical appearances of yellow fever.

Bennett and his co-workers have recently repeated this test with four additional monkeys. After being bitten by presumably infected neo-arctic mosquitoes, the four monkeys showed no febrile reaction. Two of them, however, died of yellow fever between the tenth and the thirteenth day. Control intracerebral inoculation of mice with mosquito emulsions showed that 60 per cent of the mosquitoes which had bitten an infected monkey fifteen days previously were carriers of yellow fever. It is nevertheless suggestive that the two monkeys which developed no symptoms had been bitten by mosquitoes kept from fourteen to fifteen days at 28 C., while the two monkeys which died had been bitten by mosquitoes incubated at 37 C. (98.6 F.).

When subtropical mosquitoes are used to infect monkeys with yellow fever there is a usual incubation period of from three to four days, followed by a sharp rise in temperature (104 to 105 F.) lasting from thirty-six to forty-eight hours. This is followed by subnormal temperature and collapse, death almost invariably taking place on the fifth or sixth day. The prolonged incubation period in the Harvard tests, therefore, suggests that the virus of yellow fever is attenuated in the bodies of neo-arctic mosquitoes. Of particular hygienic interest is the evidence that temperature plays an important part in determining vector infectivity. Somewhat analogous temperature effects have been described for subtropical mosquitoes. This result suggests that low temperature rather than the absence of available insect carriers is the main factor limiting the spread of yellow fever in northern states.

2. Smith, J. B.: Report of the New Jersey State Agricultural Experimental Station, Trenton, New Jersey, MacCrellish and Dingley, State Printers, 1904.

Current Comment

TRAFFIC IN OPIUM

With the submission of the report of the Advisory Committee on Traffic in Opium and Other Dangerous Drugs [1] to the Council of the League of Nations, a new and important stage of work in the suppression of the abuse of narcotics appears to have begun. The committee framed a definite statement of the essential principles which might serve as a basis for a future convention on limitation and indicated that this future convention will render possible a final suppression of the use of opium for smoking in countries or territories where the practice is still authorized. Its main purpose will be to develop appropriate measures for a gradual reduction of the quantities of raw opium required for the manufacture of prepared opium. The report of the preparatory committee, which was adopted by the advisory committee, stated as a premise that opium is being produced in quantities far in excess of recognized world requirements. The world requirements of raw opium for purposes recognized in the convention should be ascertained by a system of government estimates similar to that applied under the previous limitation convention. In furnishing such estimates governments would have to state not only the quantities but also the qualities (morphine content) of the opium required. A definite quantitative limit should be fixed annually for the amount of raw opium to be produced by each country. This should be achieved by estimating the requirements and by government agreements not to exceed the estimates in their imports. Estimates of production and requirements should be examined by an international control authority which should have the task of allocating to each producing country on the basis of the estimates the annual quantities to be produced and exported. Furthermore, the convention should consider the methods of regulating stocks of raw opium to be kept in producing and consuming countries and provisions should be made for safeguarding the carrying out of the convention by means of national control. The application of the convention, as in the case of the limitation convention in 1931, should be supervised by an international body entrusted with such powers and duties as shall be specified in the convention. The success of the limitation convention in 1931 has been such as to indicate that this properly international problem of control is now approaching its final phase. While the United States is not a signatory of the League, it has been represented at all the conventions and has ratified all but the 1925 convention for opium control.

1. Report to the Council: Advisory Committee on Traffic in Opium and Other Dangerous Drugs, League of Nations, Geneva, June 24, 1938.

ORGANIZATION SECTION

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

The Council on Medical Education and Hospitals held its usual fall meeting in Chicago on December 4.

REPORT ON PROGRAM OF FEBRUARY CONFERENCE

A report was made on the program for the next Annual Congress on Medical Education and Licensure to be held in Chicago in February.

VISITS TO MEDICAL SCHOOLS

Reports of recent visits to medical schools were also considered. The Council noted the progress that had been made toward the preparation of a final report on the survey of medical schools which it is planned to publish in the spring or early summer.

ACTION ON UNIVERSITY OF ARKANSAS MEDICAL SCHOOL

The University of Arkansas School of Medicine, by vote of the Council, is now listed as being on probation.

ACTION ON VERMONT AND VIRGINIA COLLEGES

A review of conditions at the University of Vermont College of Medicine and the Medical College of Virginia was postponed until the next academic year.

APPROVAL OF CERTIFYING BOARD IN ANESTHESIOLOGY

The American Board of Anesthesiology was approved.

COOPERATION WITH CERTIFYING BOARD IN RADIOLOGY

A plan of cooperation which had been prepared by the Council and the American Board of Radiology was endorsed and it was recommended that other special examining boards be invited to participate in similar plans.

CONSIDERATION OF HOSPITALS

The usual lists of hospitals desiring registration, intern approval and residency approval were presented and acted on.

CONFERENCE ON COOK COUNTY HOSPITAL

Representatives of the staff of the Cook County Hospital were informed that, while there has been no change in the status of the Cook County Hospital, the Council appreciates the efforts which have been made to improve conditions and the willingness of the executive committee to cooperate with the Council in further efforts to make it an outstanding center of medical education.

ACTION ON HOSPITALS APPROVED FOR INTERNSHIP

The Essentials of a Hospital Approved for the Training of Interns were amended so that after Jan. 1, 1940, a minimum of thirty-six necropsies a year will be required, and for a service having 2,000 annual admissions at least three interns will be deemed necessary.

APPROVED RESIDENCIES

The scope of the Council's list of approved residencies was broadened and its title hereafter will be "Approved Residencies and Fellowships."

The Council voted that at least one year's training in general surgery should be a prerequisite for approved residencies or fellowships in such subdivisions of surgery as urology, orthopedic and thoracic surgery.

MEETING WITH ADVISORY COMMITTEE

The Council on Medical Education and Hospitals conferred also with a newly appointed advisory committee. Those present included Drs. Ray Lyman Wilbur, J. H. Musser, Fred Moore, Reginald Fitz, Charles Gordon Heyd, Frank H. Lahey, William D. Cutter, Malcolm T. MacEachern, John R. Neal, Charles B. Pinkham, William P. Wherry, Herman G. Weiskotten, Rock Sleyster, Olin West, Morris Fishbein, Oswald N. Andersen, Fritjof H. Arestad, Hamilton H. Anderson and Mr. Homer F. Sanger.

WILLIAM D. CUTTER, M.D., Secretary.

AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

Jefferson County, Alabama

The Jefferson County Medical Society report of the Survey of the Need and Supply of Medical Care is so complete in all its phases as to deserve special mention.

Jefferson County occupies an area of 1,124 square miles in the north central portion of Alabama. It has an estimated population of 477,100, of which approximately 38 per cent are Negroes. The city of Birmingham has a population of 289,700, and the two next largest cities, Bessemer and Fairfield, have populations of 21,700 and 13,300 respectively. In addition there are seven other cities and villages with populations varying from 466 to 7,341. Jefferson County is largely dominated by the iron and steel industries.

The county medical society not only conducted the study in an exceptionally thorough manner but also made a careful and scholarly analysis of the facts. The report of the study and the recommendations filled 131 typewritten pages, which have been permanently bound for future reference. The summary and conclusions which follow are given exactly as they were prepared by the committee in charge of the study.

SUMMARIZED REPORT OF THE SURVEY

The following report covers the more important details, determined by actual survey, and summarizes the original 140 page report prepared by the secretary of the committee. The procedures used for the collection of data were those outlined by the American Medical Association. The information obtained includes and supplements that requested by the American Medical Association and is intended to furnish the society with all the pertinent facts relative to the problems involved.

The sources of information which form the basis of this study are given in table 1.

The fact that only 58 per cent of all physicians and dentists answered their questionnaires, as compared to 100 per cent of the various agencies, does not necessarily indicate that the professions were the least interested in the survey. The difference is partially accounted for by the manner in which the data were collected. When agencies did not respond by mail the proper parties were interviewed personally. This procedure was not possible with physicians and dentists. Because of their large number, contact was entirely by mail and by telephone.

Due credit should be given to the various welfare, relief and health agencies for their willingness to furnish all available information; of all the groups approached they appeared to be the most interested and most cooperative.

TABLE 1.—*Distribution of Questionnaires*

	Number Sent	Number Returned	Per Cent Returned
Physicians and dentists	586	342	58.3
Hospitals	14	14	100
Nursing organizations	3	3	100
Health departments	1	1	100
Welfare, relief and unofficial health agencies	37	37	100
School systems	6	6	100
Colleges	3	3	100
Other organizations (chiefly industrial)	74	74	100
Pharmacists	171	171	100
Totals	895	651	72.7

TABLE 2.—*Questionnaires from Physicians and Dentists*

	Number Sent	Per Cent Returned
Physicians, total	438	64.4
Members of county medical society	352	68.2
Nonmembers of county medical society	86	48.8
Dentists	148	40.5
Total physicians and dentists	586	58.3

PHYSICIANS AND DENTISTS

There are in Jefferson County 438 physicians and 148 dentists engaged in active practice. This excludes those who have retired and a few who are completely occupied in administrative capacities. There is one physician for each 1,089 of the general population.

The nature of the data requested of members of both professions precludes the presentation of actual figures; only estimates are available, though it is felt (after checking the reports made by physicians with those from the various institutions and agencies) that these estimates are conservative and probably considerably understate the facts.

Returns were received as shown in table 2.

If the data, based on actual reports of 64.4 per cent of all practicing physicians and 40.5 per cent of all practicing dentists, are truly representative of medical and dental practice in this locality, the figures obtained can appropriately be extended to include all those who have not returned their questionnaire. When such figures are combined with data obtained from all the various institutions and agencies, the total charity load may be conservatively estimated as in table 3.

Approximately one half of charity patients applied directly to physicians and dentists and received free treatment, while one half were treated in hospitals and clinics. These figures definitely indicate that the charity load of physicians in home and office practice is fully as great as the charity load carried by physicians in all institutional practice, including hospitals, outpatient departments and clinics of all the various agencies.

Besides the incalculable number of hours given by physicians in the medical care of hospital inpatients, they devoted an estimate of 41,000 hours to the free care of ambulatory cases in outpatient departments and dispensaries and to preventive medical care in various health centers and clinics. For all this they received nothing except nominal compensation for approximately 5 per cent of their time.

Seventy four per cent of physicians perform preventive medical services. Of ninety physicians reporting on the amount of preventive medical work done for charity and for pay, 37 per cent stated that they did no charity work, 25 per cent reported that less than 50 per cent of their preventive medical services were for charity, while 38 per cent reported that more than 50 per cent of such work was for charity.

Compensation for preventive medical services (in significant amounts) is made by only two organizations. The health department paid $4,054 to forty-two physicians and $948 to eighteen dentists for 2,054 hours of work in health centers. The Anti-Tuberculosis Association paid $1,305 to five physicians for clinic sessions. With minor exceptions all other medical and preventive medical services were performed by physicians without remuneration.

DENTISTS

The participation of dentists in this study has been disappointing. Questionnaires were sent to all 148, but only 40.5 per cent replied. Many of these were incomplete.

The amount of charity work done by dentists cannot be estimated very closely, but on the basis of individual information it appears that the charity load of the individual physician is more than twice that of the individual dentist. The charity load of all physicians is probably more than eight times that carried by all dentists.

TABLE 3.—*Total Charity Load of All Physicians and Dentists*

	Patients	
	Number	Distribution
Home and office practice	54,650	54.3%
Hospital inpatient practice	12,678	12.6%
Outpatient and clinic practice	33,251	33.1%
Total	100,579	100.0%
Cared for by physicians	88,131	87.6%
Cared for by dentists	12,448	12.4%

TABLE 4.—*Availability of Medical Care*

	Physicians and Dentists	
	Number	Per Cent
Present facilities and methods for providing medical care are adequate; no change indicated	32	21
More adequate provisions are needed to furnish medical, dental or hospital care to low income groups and to the indigent	76	50
Other comments not pertinent to foregoing classification	45	29
Total	153	100

AVAILABILITY OF MEDICAL CARE

Of physicians and dentists commenting on the availability of medical care, 80 per cent knew of no instance in which persons had been unable to obtain medical,

dental or hospital care. Twenty per cent reported instances in which persons were unable to obtain such care.

The majority of physicians expressed some opinion regarding the adequacy or inadequacy of present methods and facilities for providing medical care. The interpretation of these opinions has been difficult, and for that reason the data should be regarded as only an approximation.

The most frequent comment made was an expression of the need for a part pay clinic and hospital for the low income group which would also provide for the specialized services such as x-ray and biopsy free or at reduced rates.

TABLE 5.—*Charity Hospital Services*

Hospital	Number of Indigent	Per Cent of Total
County Hospital	10,855	85.6
Children's Hospital	736	5.8
Norwood Hospital	350	2.8
Children's Home Hospital	232	1.8
Jefferson Sanatorium	225	1.8
St. Vincents Hospital	184	1.4
Salvation Army Hospital	71	0.6
West End Baptist Hospital	25	0.2

TABLE 6.—*Services Performed by Nursing Organizations*

	Nurses	Patients Served	Per Cent of Patients Served as Charity
Private duty nurses (Nurses' registry only)	208	5,712	0.8
Public health and visiting nurses			
Health department	41	22,187	100
Metropolitan Life	5	2,012	0
Total	208	29,911	55.7

HOSPITALS

There are in Jefferson County fourteen hospitals with a total capacity of 1,689 beds, or 3.5 beds per thousand of the population.

Hospital rates vary from a low of $1.50 a day for ward beds to a high of $10 a day for private rooms. These rates are not excessive.

Of a total of 41,000 patients cared for in local hospitals, 31 per cent were for charity. The average stay of pay patients in hospitals was 8.7 days, as compared to an average stay of 12 days for charity patients.

The load of charity hospital services was carried as shown in table 5.

Six hospitals operate outpatient departments or associated clinics and served 37,710 persons, of whom 18,081 were charity patients.

As regards inpatient services, most pay hospitals report the rejection of patients because of their inability to pay or because beds were not available. The number of persons rejected cannot be determined.

The County Hospital reports a need for 100 additional beds. All hospitals emphasize the need of providing for hospitalization of contagious diseases. As regards sanatorium beds for the treatment of tuberculosis there are now available for white persons only 72 per cent, and for Negroes only 5 per cent of those considered necessary for this county.

Group hospital insurance seems to have been an important factor in Jefferson County in making hospital care available to the general public, though there is no indication that it has served to lighten the load of charity hospital service. Of an estimated number of 62,375 persons carrying hospital insurance providing complete or practically complete coverage, approximately 11,000 carry insurance through the Hospital Service Corporation and the remainder through various industrial arrangements.

NURSING SERVICES

Services performed by the various nursing organizations may be summarized as in table 6.

The number of private duty nurses available through the nurses' registry, though small, appears adequate to serve those patients who can afford to pay for nursing services. There is one public health nurse for each 12,000 of the general population; accepted standards for good public health practice call for one nurse for each 2,500 of the population.

Nurses comment on the lack of provision for hospitalization of cases of contagious disease. Of a total of 3,653 contagious disease patients receiving some nursing care, 3 per cent were served by private duty nurses, the remainder by public health and visiting nurses. Approximately 65 per cent of the 22,187 individuals served by the health department nurses were clients of the department of public welfare.

HEALTH DEPARTMENT

Time does not permit an adequate summation of the work of the health department; furthermore, the general familiarity of the profession with the nature of its services makes this unnecessary.

In 1937 the health department employed 113 persons in maintaining the following services: administration, records and vital statistics, laboratories, health education, food control, sanitation, child and maternal hygiene, public health nursing, and school health education.

Table 7 briefly outlines some of the major activities.

TABLE 7.—*Major Activities of Health Department*

1.	8,627	births and 5,892 deaths recorded
	8,110	transcripts issued
2.	73,866	specimens (of value in the diagnosis of infectious diseases) were examined for physicians of Jefferson County
	10,143	specimens of food and 3,087 samples of water from public water supplies examined
		The commercial value of this laboratory work by conservative estimate amounted to 1½ times the cost of operating the entire health department
3.	5,049	inspections of retail food establishments
	171,758	veterinary inspections of animals slaughtered at packing houses
	15,554	dairy inspections
	230,000	pounds of food condemned
	27,622	improvements effected
4.	22,685	sanitary inspections of public and private premises
	6,670	nuisances abated
	1,596	toilet facilities improved or installed
	631	cases of contagious diseases isolated
	1,732	contacts quarantined
5.	954	public lectures given
	1,132	moving pictures shown
	52	radio talks given
6.	53,804	visits by nurses to 22,187 persons
	12	maternal and child hygiene, and 4 dental clinics operated serving 8,070 persons who were seen by physicians or dentists

The health department is well organized and its activities are well conducted. Its usefulness, however, is greatly limited through lack of funds. The committee does not feel that a detailed report of the financial needs of the health department is pertinent to the present discussion except to state (1) that expenditures for public health in Jefferson County are not only small but fall more than 50 per cent short of the

requirements for a minimum program which may be consistent with safety and (2) that, while state subsidy to Jefferson County for county health work has increased in recent years, such subsidy on a per capita basis is still only 50 per cent of that allocated to other counties and should be increased.

A detailed discussion of the financial status of the health department has been submitted to the board of censors for its information and for such action as it may deem appropriate.

PRIVATE AND GOVERNMENTAL WELFARE, RELIEF AND UNOFFICIAL HEALTH AGENCIES

Of the thirty-seven agencies included in the category of private and governmental welfare, relief and unofficial health agencies, twenty-seven are financed by the community chest. Fourteen agencies either arrange for or furnish medical or dental care. Ten arrange for or provide care in physicians' or dentists' offices, while six arrange for or provide care in the home. Eleven agencies attempt to arrange for hospital services, though none should be considered as actually doing so as most hospitals have their own rules for accepting patients regardless of who may refer them for care. Seven agencies provide limited supplies of drugs.

Clinics are maintained as shown in table 8.

TABLE 8.—*Clinics Maintained by Agencies*

	Number of Visits *
Department of public welfare	1,890
Antituberculosis association	3,911
Fresh air farm	350
Juvenile court	1,500
Trinity community house	3,131
Total clinic visits	10,782

* All numbers are estimated

Those agencies which operate clinics render a direct service. Most others seek medical care for their clientele by requesting physicians to render services without charge or by utilizing other charity institutions. The more important charity organizations which carry the great bulk of the charity load, and which are most commonly utilized by all the various agencies are the antituberculosis association, children's hospital and clinic, county hospital and clinic and the health centers of the health department.

It is estimated that approximately 7,100 persons were provided with care through direct efforts of all the various social agencies. They report a total of 1,270 persons for whom care could not be obtained; 1,100 of these were reported by the department of public welfare.

DEPARTMENT OF PUBLIC WELFARE

Because of its importance, special mention should be made of the department of public welfare. During the year 1937 the department averaged approximately 4,000 families who received financial assistance. These were made up of those over 65 years of age, households with children under 16 where there was no employable head of the family, and those entirely physically or mentally handicapped to earn a living. The case load represents a high percentage of individuals having physical disabilities.

Because of limited funds, appropriations for prescriptions, drugs, visits of physicians and medical appliances must all be kept on the same inadequate basis as the monthly grants, which in their entirety are below the subsistence level for food.

A total of $1,308 of city-county funds was expended for maintenance of a medical office in Birmingham, while $1,585 in city-county funds was expended in maintaining a clinic in Bessemer; to the latter the Works Progress Administration added $3,911. The total expenditures by the department of public welfare (from all sources) was $6,804 for the medical care of the sick in 4,000 families. Of this total physicians received $289.

Provisions for home and office visits of physicians are for emergency cases only and are entirely inadequate to meet the medical needs of persons on relief. The clinic facilities in Bessemer are, of course, available only to persons on relief who live in that district. Under the circumstances it is not surprising that medical care was not obtained for an estimated number of 1,100 persons.

SCHOOLS

There are six school systems with a total enrolment of 103,000. Two systems with approximately half this enrolment provide for medical and dental inspection of pupils. In the other four systems the health status of the child rests with the teacher or public health nurse, and arrangements for medical examination and care must be made through family physicians, clinics, health centers or other means as circumstances permit. One failure of existing school health programs lies in the inability to make medical examinations at regular intervals. As a result many defects which might be corrected through private or public means are never discovered. Furthermore, facilities are not available to follow up properly those children who need corrections in an effort to see that they are obtained.

MEDICAL CARE IN INDUSTRIES

Forty-nine establishments provide medical care of employees only in case of accidents. Twenty-two firms furnish complete medical care for approximately 190,000 employees and dependents. With minor exceptions medical care provided by industries is judged to be adequate. Of the employees of all companies which provide complete medical care, 92.3 per cent have free choice of physician and may elect medical care by fee deduction or in two instances may accept such services from the company without cost to themselves. Approximately 2,900 individuals are given medical care through mutual benefit associations or by similar arrangements.

PHARMACISTS

The reports from pharmacists are not sufficiently reliable to merit attention. Of interest, however, was their comment regarding the needs for medical care.

Of seventy-nine pharmacists making comment, four considered present facilities for medical care adequate; three made miscellaneous comment. Seventy-two favored a change in methods or facilities for providing medical care and thirty-two of these favored some unspecified form of governmental control, four advocated utilization of the community chest, while thirty-six offered no plan or suggestion.

NEEDS FOR MEDICAL CARE

Physicians and dentists in home, office and institutional practice, on very conservative estimate, cared for from 100,000 to 116,000 charity patients. Despite this tremendous charity load carried by the professions, it

appears that present facilities are inadequate and that many needy persons were unable to obtain medical care.

The actual number of persons unable to obtain such care cannot be determined with accuracy. What is perhaps more important than arriving at the actual number is an appreciation of those circumstances under which medical care is ordinarily not available.

There is no great difference of opinion between physicians, dentists and the various social and health agencies as to the inadequacies of facilities and the present circumstances under which medical care is not available. These inadequacies are expressed in the following recommendations made by these groups in answering questionnaires.

The most commonly expressed opinions of physicians, dentists and the various social agencies for additional needs are:

1. Part pay clinics and hospital for the low income group.
2. Dental clinics (performing preventive and restorative services for the indigent).
3. Provisions for home care of the indigent and follow-up care of those discharged from hospitals. Also ambulance service to charity hospitals for the critically ill.
4. Better facilities for the treatment of syphilis.
5. Provision for hospitalization of contagious disease cases.
6. More sanatorium beds for the treatment of tuberculosis.
7. More adequate provision for the care of transients and nonresidents.
8. Increased facilities at Hillman Hospital and clinic, larger social service staff.
9. Increased facilities of health department.

The various agencies also expressed the following opinions which were not commonly expressed by members of the professions. Need for:

1. Payment through public funds of physicians and dentists for home, office and institutional care of the indigent.
2. A centralized social service bureau to serve all agencies.
3. Provision for health examination of persons over 12 years of age.
4. Psychiatric clinics; more adequate hospital provisions by the state for the care of mental cases.
5. More adequate provision for drugs, teeth, eyeglasses and so on.
6. Child guidance clinic.
7. Ear clinic for the treatment and prevention of hearing defects.
8. Better organization of medical resources.

RECOMMENDATIONS

1. The committee endorses in principle a part pay hospital and clinic for the low income group, which group it designates as those whose income level is just above that established by the Hillman Hospital in its "basic guide for determining indigency."

2. In order to differentiate between charity, part-pay and pay patients the committee feels that it will be essential to establish a dignified and efficient business bureau with a social service department to investigate thoroughly the financial status of patients. This should be a centralized service functioning for all charity and part-pay institutions including the Hillman Hospital and clinic, department of public welfare, health department and others.

3. The committee recognizes the total inadequacy for hospital care of cases of contagious disease (both pay and indigent) and feels that some provision should be made.

4. The committee feels that local appropriations for public health in Jefferson County are not only small but fall 50 per cent short of the requirements for a minimum program. Furthermore, state subsidy to Jefferson County for county health work, on a per capita basis, is only 50 per cent of that granted to other counties and should be increased.

[The remainder of the report deals with a local hospital and a special "Proposed Plan for the Medical Care of the Indigent and Low Income Groups."]

OFFICIAL NOTES

JUDGE PROCTOR OVERRULES MOTION TO QUASH SECOND SUBPENA

Following Judge James M. Proctor's quashing of two thirds of a subpena requiring the American Medical Association to present before the Special Grand Jury certain records, some extending as far back as sixteen years, the Department of Justice revised the subpena. The revised subpena would command to bring: All . . . documentary communications and all reports or memoranda . . . containing statements with respect to any action or policy taken or adopted or considered or proposed to be taken or adopted by or on behalf of the A. M. A. or of any medical society or association affiliated with the A. M. A., or of any hospital, in opposition to group medical practice or to the provision of medical care on a periodic prepayment basis, drawn up, sent or received from Jan. 1, 1935, to Nov. 20, 1938, by certain officials at the headquarters of the association, its judicial council, its bureau of investigation, and any other official employee of the association who, according to the present knowledge of the officials, drew up, sent or received such papers.

Counsel for the American Medical Association argued before the court that the present order was so broad that it was void. Counsel also quoted a decision by Justice Holmes of the United States Supreme Court to the effect that it was "contrary to first principles of justice" for a grand jury to go deeply into records of a corporation "in the hope that something will turn up."

In overruling the motion to quash the revised subpena, Justice Proctor is reported to have set down the following memorandum opinion:

A recent subpena duces tecum to the American Medical Association was partially quashed, as unreasonable and oppressive because of its sweeping requirements. This subpena is intended to overcome those faults. I think it does so.

The desired papers are well identified. The periods of time to be covered by the search, although longer than the statutory period of limitation, are definitely fixed, and not necessarily unreasonable, having in mind the nature of the inquiry. The papers required, it is understood, are only those which may now be in possession of the association or its officers.

I see no reason why the association cannot comply with the subpena without undue difficulty or hardship, if its papers have been kept under any efficient system of filing.

Counsel for the association again contend that the papers described by the subpena are irrelevant and incompetent to the subject matter of the inquiry before the grand jury and that the matters being investigated cannot by their nature involve any violation of the Sherman Antitrust Act, in respect of its local or interstate provisions. It is therefore argued that as the investigation concerns matters of which this court would have no jurisdiction, the proceeding cannot legally form the foundation for issuance of the subpena. It is insisted that the court should now determine these basic questions.

I cannot agree with these contentions. The virtual effect of the propositions to now pass upon the admissible quality of evidence sought for production before the grand jury, or produced before it, and to determine vital questions of jurisdiction, would be to require a close and detailed supervision by the court of the grand jury process in this investigation which, I think, can find no proper support in the historical background and development of the grand jury system, or the well established rules of criminal procedure. Moreover, the present inquiry before the special

grand jury is of an original nature. Neither the American Medical Association nor any other party has been held for action of the grand jury upon any criminal charge. The inquisition has its origin with the grand jury. There are as yet no defendants. There may never be any. Hence, at this stage of the proceedings, the association has no such status as entitles it to raise any of the vital questions now urged upon the court.

In my opinion, the motion to quash the subpena should be overruled, and it is so ordered.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

The Annual Congress of the Council on Medical Education and Hospitals of the American Medical Association will be held at the Palmer House, Chicago, Feb. 13 and 14, 1939. The Federation of State Medical Boards of the United States will participate in the Congress. The program follows:

Monday Morning, February 13

The Protection of the Public Through the Activities of the Council on Medical Education and Hospitals
Ray Lyman Wilbur, M.D., LL.D., Chairman, Stanford University, Calif.

(Subject to be Announced)
James B. Conant, Ph.D., President, Harvard University, Cambridge, Mass.

The Organization and Subject Matter of General Education
Robert Maynard Hutchins, LL.B., President, University of Chicago.

(Subject to be Announced)
Walter F. Donaldson, M.D., Secretary, Medical Society of the State of Pennsylvania, Pittsburgh.

Canadian Experiments in Medical Economics
T. C. Routley, M.D., LL.D., General Secretary, Canadian Medical Association, Toronto, Ont.

Monday Afternoon, February 13

The South as Testing Ground for the Regional Approach to Public Health and Public Welfare
Howard W. Odum, LL.D., Director, Institute for Research in Social Science, University of North Carolina, Chapel Hill.

SYMPOSIUM ON THE SMALL HOSPITAL

Organization and Management of the Small Hospital
Malcolm T. MacEachern, M.D., Associate Director, American College of Surgeons, Chicago.

The Community Hospital
Barry C. Smith, General Director, The Commonwealth Fund, New York.

The Planning and Organization of the Small Hospital
William Henry Walsh, M.D., Consultant Specialist on Hospitals, Chicago.

The Construction of the Small Hospital
Carl A. Eriksen of the firm of Schmidt, Garden and Eriksen, Architects, Chicago.

Tuesday Morning, February 14

The Program of the National Committee for Mental Hygiene
Clarence M. Hincks, M.D., General Director, National Committee for Mental Hygiene, New York.

Federal Support of Professional Education
Dean Lewis, M.D., Surgeon-in-Chief, Johns Hopkins Hospital, Baltimore.

Fundamentals of Industrial Hygiene
T. Lyle Hazlett, M.D., Professor of Industrial Hygiene, University of Pittsburgh School of Medicine and Medical Director, Westinghouse Electric and Manufacturing Company, Pittsburgh.

The Relation of Anesthesiology to Medical Education
Ralph M. Waters, M.D., Department of Anesthesia, University of Wisconsin Medical School, Madison.

Tenure of Members of the Faculty in Schools of Medicine
Anton J. Carlson, Ph.D., Frank P. Hixon Distinguished Service Professor of Physiology, University of Chicago.

Tuesday Noon, February 14

Luncheon meeting, to which all those attending the Congress are invited to attend.

Address: *What the Undergraduate College Should Give the Future Doctor*
William Mather Lewis, LL.D., President, Lafayette College, Easton, Pa.

Monday Evening, February 13

FEDERATION DINNER

(Program to be announced later.)

Tuesday, February 14

THE FEDERATION OF STATE MEDICAL BOARDS OF THE UNITED STATES

(Program to be announced later.)

THE ST. LOUIS SESSION

Special Exhibits on Fractures and on Anesthesia in the Scientific Exhibit

The Committee on Scientific Exhibit of the Board of Trustees has announced two special features for the St. Louis session, May 15-19, 1939.

The Special Exhibit on Fractures will be presented as at former annual sessions under the supervision of a committee the members of which are Dr. Kellogg Speed, Chicago, chairman; Dr. Frank D. Dickson, Kansas City, Mo., and Dr. Walter Estell Lee, Philadelphia.

The Special Exhibit on Anesthesia will be presented for the third year under the supervision of a committee composed of Dr. Ralph M. Waters, Madison, Wis., chairman; Dr. John S. Lundy, Rochester, Minn.; Dr. Henry S. Ruth, Philadelphia, and Dr. Philip D. Woodbridge, Boston.

Application blanks for space for other exhibits may be obtained from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

COMMITTEE OF PHYSICIANS MAKES NEW RELEASE

The Committee of Physicians for the Improvement of Medical Care, Inc., issued for release on December 3 a statement signed by Dr. John P. Peters and said to express the point of view of the committee in relationship to the National Health Program.

WITNESSES BEFORE THE GRAND JURY IN WASHINGTON

The following additional witnesses are reported to have appeared before the Special Grand Jury in Washington, D. C.: Dr. Harry Clifford Loos of the Ross-Loos Medical Group, Los Angeles, and Dr. George R. Stevenson of the San Diego Beneficial Society, San Diego, Calif. Dr. Michael A. Shadid of Elk City, Okla., said to be the founder and medical director of the Farmer's Union Cooperative Hospital Association, and Mr. F. D. Kilpatrick, said to be a labor leader of Akron, Ohio, who is organizing the Summit County Cooperative Health Association.

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks.

The program is broadcast each Wednesday over the Blue network of the National Broadcasting Company at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).[1]

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 14. What Shall We Eat?
December 21. Hidden Treasures in Foods.
December 28. Good Milk, Good for You.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARIZONA

Plague Infection in Prairie Dogs.—According to *Public Health Reports*, plague infection has been proved in a pool of ninety-eight fleas collected from eighteen prairie dogs (Cynomys gunnisoni zuniensis) shot September 27 seven miles south of St. Johns, Apache County.

ARKANSAS

Seventeenth Clinical Meeting.—The Fort Smith Clinical Society held its seventeenth meeting in Fort Smith October 11 under the auspices of the clinical staffs of St. Edwards Mercy and Sparks Memorial hospitals. The speakers included:

Dr. George V. Brindley, Temple, Texas, Treatment of Acute Perforated Appendicitis and Peptic Ulcer, Its Complications and Indications for Surgical Treatment.
Dr. Sidney J. Wolfermann, The Advantages of Vitallium in Bone Fixation.
Dr. William R. Brooksher, The Painful Shoulder.
Dr. Paul M. Bassel, Temple, Thyroid Dysfunction.
Dr. Charles T. Chamberlain, The Heart and Obesity.
Dr. James H. Buckley, Differential Diagnosis of Acute Conjunctivitis, Iritis and Glaucoma.
Dr. Arless A. Blair, Treatment of Underweight in Nondiabetic Individuals with Protamine Zinc Insulin.
Dr. James W. Amis, Use of Sulfanilamide in Undulant Fever.
Dr. Arthur F. Hoge, Factors in Mortality of Appendicitis.

COLORADO

Midwinter Graduate Clinics at Denver.—The midwinter graduate clinics, sponsored by the Colorado State Medical Society, will be at the Shirley-Savoy Hotel, Denver, December 14-16. The clinics are open to all doctors of medicine in the Rocky Mountain region regardless of membership in any medical society. The guest speakers will include:

Dr. Arlie Ray Barnes, Rochester, Minn., professor of medicine, University of Minnesota Graduate School of Medicine.
Dr. Rollin Russell Best, Omaha, Neb., assistant professor of anatomy and surgery, University of Nebraska School of Medicine.
Dr. Horton Ryan Casparis, Nashville, Tenn., professor of pediatrics, Vanderbilt University School of Medicine.
Dr. Everett Dudley Plass, Iowa City, professor of obstetrics and gynecology, State University of Iowa College of Medicine.
Dr. James E. M. Thomson, Lincoln, Neb.

ILLINOIS

Tri-County Meeting at Galesburg.—The Knox County Medical Society was host at a meeting with the Henry and Warren county medical societies in Galesburg October 25. The speakers included:

Dr. Warren H. Cole, Chicago, Hyperthyroidism.
Dr. Claire LeRoy Straith, Detroit, First Aid Treatment of Automobile Injuries to the Face.
Dr. William P. Murphy, Boston, The Practical Management of the Anemic Patient.

Dr. Arthur E. Hertzler, Halstead, Kan., as the after dinner speaker, discussed "Hooks, Bobs and Sinkers." Dr. Logan Clendening, Kansas City, also spoke.

Chicago

Hospital News.—The National Jewish Hospital, a tuberculosis sanatorium, Denver, has recently established an office in Chicago at 30 North La Salle Street.

Personal.—Dr. Paul R. Cannon, professor of pathology, University of Chicago, has been appointed a member of the Medical Fellowship Board of the National Research Council, for the period ending June 30, 1941, to complete the unexpired term of Dr. Eugene L. Opie, New York, who resigned.

Society News.—At a meeting of the Chicago Neurological Society October 20 the speakers were Drs. Foster Kennedy, New York, on "The Organic Background of Mind"; Victor E. Gonda, "War Neuroses," and Paul C. Bucy, "Tremor: A Consideration of Its Physiology and Abolition by Surgical Means."——The Chicago Ophthalmological Society was addressed October 24 by Drs. Samuel G. Higgins, Milwaukee, on "Ophthalmic Surgery in India" and William A. Fisher, "Senile Cataract: The Usual Method of Operating in India." Dr. Robert von der Heydt showed photographs in color of diseases of the eye.——Dr. Howard C. Taylor Jr., New York, discussed "Relationship of Hormones to the Toxemias of Pregnancy" before the Chicago Gynecological Society November 18.——The Chicago Orthopaedic Society was addressed November 11 by Drs. Walter R. Fischer on "Fracture of the Scapula Requiring Open Reduction" (report of a case) and Wallace H. Cole, St. Paul, "Clinical Observations on the Physiology of Bone."——Dr. Gilbert J. Thomas, clinical associate professor of urology, University of Minnesota Medical School, Minneapolis, discussed "Tuberculosis of the Urological Tract" before the Chicago Medical and Urological societies at a joint meeting December 7 at the Chicago Woman's Club.

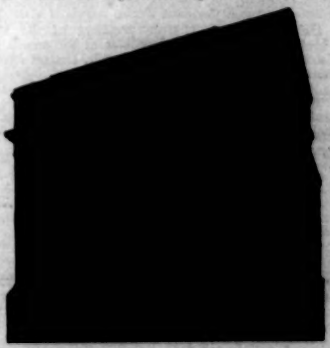
IOWA

Personal.—Rev. G. T. Notson resigned as superintendent of the Methodist Hospital, Sioux City, October 21; he has held the position since the hospital was founded eighteen years ago.——Dr. Edward N. Anderson, Boston, has been appointed head football coach at the State University of Iowa, Iowa City, following his resignation from a similar position at Holy Cross College, Boston. Dr. Anderson graduated at Rush Medical College in 1930.

Gifts to the University.—The University of Iowa College of Medicine, Iowa City, announces a gift of $22,500 from the John and Mary R. Markle Foundation to be spent over a two year period. Of the total, $12,500 will provide for a continuation of the research in the department of ophthalmology under Dr. Cecil S. O'Brien on inflammatory conditions of the eye, and the remainder will be used to continue the research program in the department of pathology under Dr. Harry P. Smith, on blood clotting and the bleeding tendency.

KENTUCKY

Memorial to Dr. Joseph N. McCormack.—Headquarters of the Kentucky State Medical Association and the State Department of Health of Kentucky were recently moved to a new home purchased by the state at 620 South



Home of State Medical Association and State Department of Health.

Third Street, Louisville, and dedicated October 4 during the annual meeting of the state medical association. The building has been made a permanent memorial to Dr. Joseph N. McCormack, first health officer of the state. Speakers at the dedicatory exercises were Drs. Carl C. Howard, Glasgow, former president of the state association, on "Joseph Nathaniel McCormack the Physician"; Gov. Albert B. Chandler, "Joseph Nathaniel McCormack the Public Servant," and Dr. Arthur T. McCormack, state commissioner of health, secretary of the state medical association and son of the elder McCormack. After the governor's address Miss Mary Tyler McCormack unveiled a portrait and a bronze plaque of her grandfather in the entrance hall of the building. The portrait was painted by Charles Sneed Williams, a Kentucky artist, and presented by the medical association. The plaque was the gift of the state department of health and of county health departments. Dr. Joseph N. McCormack was appointed state health officer when the state board of health was created in 1883 following an epidemic of yellow fever. He is said to have been instrumental in the passage of the state's first medical practice act and the first administrator of the law. Among other laws he sponsored were licensure laws, a vital statistics law and a bill

consolidating health agencies. He was chairman of the committee on reorganization of the American Medical Association, which functioned from 1901 to 1910. Dr. McCormack died Aug. 4, 1922, aged 75.

MICHIGAN

Hospital News.—Dr. Roscoe R. Graham, Toronto, lectured at Woman's Hospital, Detroit, Hospital Day, November 9; his subject was "Some Philosophic Problems Dealing with the Relation of the Fundamental Sciences to Every Day Surgical Problems."

Personal.—A testimonial dinner was held in honor of Drs. Rudolph J. Maas and William P. Scott, Houghton, by the Hancock Council of the Knights of Columbus, Hancock, October 11. Dr. Maas is 83 years old and a charter member of the council; Dr. Scott is 80, a charter member of the Houghton County Medical Society and an emeritus member of the Michigan State Medical Association.

Society News.—A symposium on ovarian tumors was presented before the Ingham County Medical Society in Lansing October 18 by Drs. Harry M. Nelson and Donald C. Beaver, Detroit.——Dr. Evan G. Galbraith, Toledo, discussed "Pulmonary Atelectasis" before the Jackson County Medical Society in Jackson October 18.——Dr. Harry A. Towsley, Ann Arbor, addressed the Washtenaw County Medical Society October 11 on "The Acute Exanthemata."——Dr. Thurman B. Rice, Indianapolis, discussed "New Concepts in Bacteriology" before the Muskegon County Medical Society in Muskegon October 28.

Thirteenth Annual Highland Park Clinic.—The thirteenth annual clinic of the Highland Park Physicians Club was held November 30 at the Highland Park General Hospital. The following program was presented:

Dr. James R. Goodall, Montreal, The Placental Blood Bank.
Dr. Eugene H. Shannon and J. A. Sullivan, M.B., Toronto, Clinical and Radiologic Aspects of Diseases of the Paranasal Sinuses.
Dr. Russell L. Haden, Cleveland, Treatment of Anemia.
Dr. Frederick Christopher, Evanston, Ill., Carcinoma of the Stomach.
Dr. Martin H. Fischer, Cincinnati, Clinical Aspects of Water Turnover.

Dr. Henry A. Luce, Detroit, president of the Michigan State Medical Society, was toastmaster at the annual banquet and Malcolm W. Bingay, editorial director, Detroit *Free Press*, was the speaker.

MISSISSIPPI

Society News.—The Delta Medical Society was addressed in Indianola October 12, among others, by Drs. Randolph T. Smith, Little Rock, Ark., on "Unusual Tumors of the Ovary" and Bernard H. Booth, Drew, "Atabrine in Malaria."——A symposium on diseases of nutrition was presented before the Issaquena-Sharkey-Warren Counties Medical Society in Vicksburg October 11 by Drs. Henry B. Goodman, Anguilla; George W. Gaines, Tallulah, La.; Hugh H. Johnston, Vicksburg, and Walter H. Scudder, Mayersville.

NEW JERSEY

Cooperative Child Guidance Program in Paterson.—A child guidance program centered about the neuropsychiatric clinic of the Paterson General Hospital has been developed in cooperation with interested agencies. The plan is to have a discussion with the specific agency that can best aid each child, with suggestions for treatment. A monthly conference is planned with each agency to study the development of the child, who is seen frequently at the clinic during the period of study. The general hospital gives its facilities to the project, and the social agencies contribute the social workers and social facilities. Among the agencies that are cooperating are the Family Welfare Society, probation authorities, criminal courts, police department, schools, churches, Church Mission Help, North Jersey Training School, the Young Men's Christian Association, Young Women's Christian Association, the Young Men's Hebrew Association and Young Women's Hebrew Association. Dr. Theodore Rothman is director of the project.

Society News.—At a recent meeting of the Monmouth County Medical Society in Asbury Park the speakers were Drs. Harold A. Kazmann, Long Branch, on "Early Symptoms of Gastrointestinal Carcinoma"; Louis F. Albright, Spring Lake, "Treatment of Pernicious Anemia," and Carlos A. Pons, Asbury Park, "Rocky Mountain Spotted Fever."——A symposium on pain low in the back was presented before the Passaic County Medical Society in Passaic October 13 by Drs. Arthur Bruce Gill, Philadelphia; William J. Mixter, Boston, and Samuel Kleinberg, New York.——Dr. Frederic E. Elliott, Brooklyn, addressed the Essex County Medical Society, Newark, November 10, on "Medical Expense Insurance."——Dr. Jesse G. M. Bullowa, New York, addressed the Bergen County Medical Society, Bergen Pines, November 8, on "The Pneumonias."——Dr. Samuel A. Loewenberg, Philadelphia, addressed the Academy of Medicine of Northern New Jersey, Newark, November 17 on "Endocrine Disturbances and Present Day Endocrine Therapy."

Committee on Health and Welfare Appointed.—Gov. A. Harry Moore has appointed a special committee to "follow up and determine applications to the needs of New Jersey of certain of the considerations brought out at the Washington Conference in July." It will be known as the New Jersey Committee on Health and Welfare. Robert C. Clothier, LL.D., president of Rutgers University, New Brunswick, is general chairman of the committee, which has fifty members, including twenty-five physicians. Six technical subcommittees were created at the organization meeting in Trenton, November 16, as follows: expanded public health facilities, hospital facilities, indigent, low wage, wage loss insurance and related matters. Twelve advisory committees to the subcommittee on expanded public health facilities were also created, as follows: advisory committee at large, maternal and child health, crippled children, blind, tuberculosis, venereal disease, cancer, pneumonia, mental diseases, industrial diseases, school health and college health.

Complete, comprehensive information on all phases of medical care in New Jersey will be assembled by this committee. The fact-finding work of the committee will include determination of what physical equipment, facilities and services are available to satisfy the health requirements of the population, determination of the incidence of degenerative diseases among groups in various income levels, determination of the adequacy of present sanitation measures and determination of what additional physical equipment, facilities, services and policies are required to assure that the health of the people will be safeguarded. Finally the committee will undertake to develop practical methods for remedying any conditions or deficiencies amenable to improvement. In the collection of this information, data accumulated in the surveys conducted by the Medical Society of New Jersey and its component county medical societies will be utilized for information on those phases of medical care which they cover.

The following physicians are members of the committee: Drs. William J. Carrington, Atlantic City, president of the state medical society; Fred H. Albee, New York; Walter G. Alexander, Orange; Leverett D. Bristol, Montclair; Charles V. Craster, Newark; Samuel B. English, Glen Gardner; George W. Fithian, Perth Amboy; Edward Guion, Northfield; Edgar A. Ill, Newark; Allen G. Ireland, Trenton; Henry Kessler, Newark; Joseph H. Kler, New Brunswick; Augustus H. Knight, Far Hills; Frederick P. Lee, Paterson; Julius Levy, Trenton; Jesse Lynn Mahaffey, Trenton; Stanley H. Nichols, Asbury Park; George O'Hanlon, Jersey City; Berthold S. Pollak, Secaucus; Ellen C. Potter, Trenton; Hilton S. Read, Atlantic City; Joseph M. Rector, Jersey City; Spencer T. Snedecor, Hackensack; Arthur L. Stone, Camden, and LeRoy A. Wilkes, executive officer of the state medical society.

NEW YORK

Rochester Academy Plans Museum.—Plans for a medical museum in the new building of the Rochester Academy of Medicine are in process of formation. Committees have been formed to develop divisions dealing with rare books and documents, plastic and graphic arts, instrument making and historical development, and pathologic anatomy. Courses of instruction for the committees have been arranged with the librarians of the city, and the university and the Rochester Museum of Arts and Sciences is cooperating. The academy wishes especially to compile the medical history of Monroe County. Dr. Morris E. Missal is secretary of the museum committee.

New York City

Third Harvey Lecture.—Dr. Eugene F. Du Bois, professor of medicine, Cornell University Medical College, will deliver the third Harvey Lecture at the New York Academy of Medicine December 15 on "Heat Loss from the Human Body."

Faculty Appointments.—New York Medical College and Flower Hospital recently announced the appointment to the faculty of Dr. Reuel A. Benson to be professor of pediatrics, James W. Benjamin, Ph.D., associate professor of histology, embryology and neuroanatomy, and Dr. David Scherf, associate clinical professor of medicine. Dr. Benjamin was formerly assistant professor of zoology at Northwestern University, Chicago, and Dr. Scherf was associate professor of medicine at the University of Vienna.

Hospital News.—A department of anesthesiology was recently opened at the Evangelical Deaconess Hospital with Drs. Henry Trautmann and Harry J. Rosenthal in charge. ——The name of the Brooklyn Home for Consumptives is to be changed to the Brooklyn Thoracic Hospital.——The Frances Schervier Hospital and Home for the Aged, built by the Sisters of the Poor of St. Francis, was dedicated November 6. It is a six story building with 404 beds. The first patients were those formerly in the St. Francis Home for Aged Incurables. ——A new wing of St. Clare's Hospital was dedicated October 30.

Society News.—A symposium on serum therapy in pneumonia was presented at the stated meeting of the New York Academy of Medicine December 1 by Drs. Russell L. Cecil, Colin M. MacLeod and Wheelan D. Sutliff.——A program on pneumonia was presented before the Bronx County Medical Society November 16 by Drs. Ralph S. Muckenfuss, John A. Colucci, Jesse G. M. Bullowa and Colin M. MacLeod.—— Dr. James T. Gwathmey addressed the Bronx Pathological Society November 15 on "Pathology of Anesthesia: Tissue Changes and the Pathologic Physiology Involved in the Use of Modern Anesthetics."——A pneumonia program was presented before the Medical Society of the County of Queens November 1 by Drs. Wheelan D. Sutliff on "The New York City Pneumonia Control Program"; Carl Boettiger, Flushing, "Early Diagnosis of Pneumonia"; Rufus I. Cole, Mount Kisco, "Serum Therapy of Pneumonia," and Colin M. MacLeod, "Antipneumococcic Rabbit Serum Therapy of Pneumonia." Dr. Alfred C. Beck addressed the society October 25 on "Syphilis in Pregnancy."

NORTH CAROLINA

Special Society Meetings.—Drs. Burton Haseltine, Chicago, and Grady E. Clay, Atlanta, addressed the North Carolina Eye, Ear, Nose and Throat Society at its annual meeting in Raleigh recently on "Chronic Sinus Infections" and "Arteriolar Changes in the Fundus Oculi; Convergent Strabismus in Children" respectively. Dr. Franklin C. Smith, Charlotte, was elected president; Dr. Henry H. Briggs Jr., Asheville, vice president, and Dr. Milton R. Gibson, Raleigh, reelected secretary.—— Dr. Vann M. Long, Winston-Salem, was elected president of the North Carolina Urological Association at its annual meeting in Greensboro October 31. Dr. John Mason Hundley Jr., Baltimore, was the guest speaker at the annual dinner, on "Physiologic and Pathologic Observations on the Urinary Tract During Pregnancy."

OKLAHOMA

New Health Officers.—Dr. Frederick E. Dargatz, formerly of Kinsley, Kan., has been appointed director of the health unit of Ardmore to succeed Dr. Richard M. Parish.—— Dr. Reed Wolfe, Sulphur, has been appointed health superintendent of Choctaw County.

Society News.—Drs. Carroll M. Pounders, Oklahoma City, and James William Finch, Hobart, addressed the Western Oklahoma Medical Society at a meeting in Hobart recently on "Rheumatic Fever in Childhood" and "Etiology of Nausea and Vomiting of Pregnancy" respectively.—Drs. J. Wendall Mercer and Evans E. Talley, Enid, addressed the Woods-Alfalfa County Medical Society, Cherokee, recently on "Prenatal Disturbances, Symptoms and Treatment" and "The Thyroid" respectively.——Drs. Rufus Q. Goodwin and Frederick Redding Hood, Oklahoma City, addressed the Garfield County Medical Society, Enid, October 27, on "Treatment of Pneumonia with Serum Therapy" and "Cardiac Irregularities" respectively.

PENNSYLVANIA

Program on Exceptional Child.—The child research clinic of the Woods Schools, Langhorne, presented its fifth institute on the exceptional child October 18. The following program was given:

Dr. Eugenia S. K. Cameron, Baltimore, Factors in the Etiology of Psychoses in Early Adolescence.
Dr. Lawson G. Lowrey, New York, Problems of Aggression and Hostility in the Exceptional Child.
Dr. Josephine H. Kenyon, New York, Stimulation of Growth in Short Children.
Edgar A. Doll, Ph.D., Vineland, N. J., Social Maturation.
May Ayres Burgess, Ph.D., New York, Height Charts in Growth Studies.

Dr. Frederick H. Allen, Philadelphia, presided at the morning session and Miles Murphy, Ph.D., Philadelphia, at the afternoon session.

Philadelphia

Plans for Third Postgraduate Institute.—The Philadelphia County Medical Society will sponsor its third annual Postgraduate Institute March 13-17, 1939, on the subjects "Blood Dyscrasias" and "Metabolic Disorders." There will be eighty-six clinical lectures with open forum discussion of each topic. Dr. Rufus S. Reeves is director of the institute. Sessions will be held at the Bellevue-Stratford Hotel.

Society News.—Dr. William Bates addressed the Philadelphia Clinical Association November 15 on "Pseudosurgical Abdomen."——At a meeting of the Philadelphia Neurological Association November 18 the speakers included Drs. Lester S. King, Princeton, N. J., on "Equine Encephalomyelitis" and George D. Gammon, "The Muscular Weakness of Family Periodic Paralysis."——Members of the department of diseases of children, Columbia University College of Physicians and Surgeons, New York, addressed the Philadelphia Pediatric Society November 8. Among the speakers were Drs. John P. Caffey, on "Syphilis of the Skeleton in Early Infancy; the Nonspecificity of Many of the Roentgen Changes," and Richard L. Day, "Effect of Sleep on Insensible Perspiration in Infants and Children."

Women Sponsor Cancer Forum.—The Women's Auxiliary of the Lankenau Hospital Research Institute and district 1 of the Pennsylvania State Nurses' Association sponsored a cancer forum November 29-30 at the Bellevue-Stratford. The guest speakers included:

Dr. William B. Wartman, Cleveland, Highlights in the History of Cancer.
Dr. James J. Durrett, U. S. Food and Drug Administration, Washington, D. C., Cancer Quacks.
Dr. Martha Edith MacBride-Dexter, Harrisburg, state secretary of health, Activities of the Pennsylvania Department of Health with Special Reference to Cancer.
Dr. William Carpenter MacCarty, Rochester, Minn., How the Pathologist Aids in Combating Cancer.
Major Julia C. Stimson, Army Nurse Corps, U. S. Army, retired, New York, The Nurses' Responsibility in Prevention and Early Recognition of Cancer.

Pittsburgh

Hospital News.—Montefiore Hospital held its annual "scientific day" November 12 with Dr. Samuel A. Levine, Boston, as the guest speaker and clinician. Dr. Levine spoke in the evening on "The Value of Auscultation."

Research on Air Filters.—Mellon Institute announces the establishment of an industrial fellowship by the American Air Filter Company, Louisville, Ky., for the study of materials of value in the construction of filters for air conditioning systems. Frank F. Rupert, Ph.D., who has been studying air hygiene at the institute since 1935, has been appointed to the fellowship.

RHODE ISLAND

Hospital Building Named for Dr. Adolf Meyer.—A new psychiatric clinic building at the State Hospital for Mental Diseases, Howard, was dedicated October 18 and named in honor of Dr. Adolf Meyer, Henry Phipps professor of psychiatry, Johns Hopkins University School of Medicine, Baltimore. The semiannual meeting of the New England Society of Psychiatry was held in the afternoon following the dedication. Dr. Meyer and Dr. John E. Donley, Providence, made addresses at the dedication exercises. An appropriate plaque was installed in the lobby of the building and Dr. Seth F. H. Howes, superintendent of the hospital, presented to Dr. Meyer a scroll commemorating the occasion. In the afternoon Dr. Meyer addressed the psychiatric society on "The Psychiatric Hospital in a Progressive Health Program." In the evening a dinner was held in honor of Dr. Meyer at the University Club in Providence, under the auspices of the Rhode Island Society for Neurology and Psychiatry. Dr. Walter C. H. Weigner, Providence, president of the society, presided and Dr. Arthur H. Ruggles, Providence, state commissioner of mental diseases, was toastmaster. The speakers included Drs. Charles Macfie Campbell, Boston, Eugen Kahn, New Haven, and Dr. Meyer. The new building is part of a $5,000,000 building program at the state hospital. It has a capacity of 120 beds and was built at a cost of $296,500.

TENNESSEE

Society News.—Drs. Edward E. Reisman Jr. and Earl R. Campbell addressed the Chattanooga and Hamilton County Medical Society, Chattanooga, October 13, on "Traumatic Injuries to the Extremities" and "Wrist Injuries" respectively. ——At a meeting of the Hardin-Lawrence-Lewis-Perry-Wayne Counties Medical Society in Lawrenceburg recently the speakers were Drs. William E. Boyce, Flatwoods, on "The

Hydrogen Ion Concentration of the Blood"; Jack Witherspoon, Nashville, "Duodenal Ulcer"; Thomas J. Stockard, Lawrenceburg, "Poliomyelitis," and Oval N. Bryan, Nashville, "Use of Antipneumococcic Serum in the Treatment of Pneumonia."

Personal.—Dr. Leonard E. Ragsdale, at one time superintendent of the State Home for the Feebleminded, Donelson, has been appointed superintendent of the Central State Hospital for the Insane, Nashville. — Dr. Malcolm T. Tipton, Union City, has been appointed a member of the state board of medical examiners to succeed Dr. Marcus G. Spingarn, Memphis, whose term expired.——Orren W. Hyman, Ph.D., dean of the University of Tennessee College of Medicine, Memphis, received the honorary degree of doctor of laws from Southwestern University, Georgetown, Texas, recently.

VIRGINIA

Changes in Health Officers.—Dr. John G. McNiel, St. Charles, has been appointed health officer of the Montgomery County health district, succeeding Dr. William W. Fuller, Christiansburg, who is studying at the Johns Hopkins University School of Hygiene and Public Health. Dr. Willard W. Griggs, St. Charles, has succeeded Dr. George R. Carpenter in the Dickenson-Wise Counties district, and Dr. Eugene B. Shepherd, Chatham, has been made health officer of the Pittsylvania County district, succeeding Dr. Benjamin Randolph Allen. Dr. Carpenter and Dr. Allen are also at Johns Hopkins. Dr. Stephen J. Beeken, Lexington, recently assistant in the Rockbridge County district, has been appointed health officer of the Russell-Tazewell district with headquarters at Richlands. He succeeds Dr. Vernon A. Turner, Richlands, who is studying at the Harvard School of Public Health.

WISCONSIN

Society News.—Dr. Karl C. Wold, St. Paul, addressed the Pierce-St. Croix County Medical Society, Baldwin, October 20, on "Common Disorders of the Eye: Their Diagnosis and Treatment."——Dr. Charles B. Puestow, Chicago, addressed the Winnebago County Medical Society, Oshkosh, October 6 on "Preoperative and Postoperative Care."

Hospital News.—St. Vincent Hospital, Green Bay, celebrated the fiftieth anniversary of its opening October 12-13 with a dinner for the staff, city and county officials and open house. —— Milwaukee Hospital, Milwaukee, celebrated its seventy-fifth anniversary during the week of October 30; from a twenty bed institution it has grown to a capacity of 263.

Personal.—Dr. Glenford L. Bellis has retired as superintendent of the Muirdale Sanatorium and Blue Mound Preventorium, Wauwatosa. Physicians and employees of the sanatorium gave a testimonial banquet to Dr. Bellis October 13 and presented him with a plaque.——Dr. Albert J. Randall, assistant director of health in Kenosha, has been appointed director to succeed Dr. Gustave Windesheim, who retired October 15.

GENERAL

Massengill Firm Fined.—Dr. Samuel E. Massengill, Bristol, Tenn., president of the S. E. Massengill Chemical Company, pleaded guilty in the federal court at Kansas City October 19 on sixty-two counts covering shipments of Elixir of Sulfanilamide-Massengill made from the Kansas City plant of the company. He was fined $9,300. In federal court at Greenville, Tenn., October 3 the defendant's counsel pleaded guilty on 112 counts and was sentenced to pay a fine of $150 for each count, making a total of $16,800 (THE JOURNAL, October 22, p. 1567).

Special Society Elections.—Dr. Edward S. Godfrey Jr., New York state commissioner of health, Albany, was chosen president-elect of the American Public Health Association at the annual meeting in Kansas City, October 25-29, and Abel Wolman, Dr.Eng., Johns Hopkins University School of Hygiene and Public Health, Baltimore, was installed as president. The following were elected vice presidents: Drs. Albert Grant Fleming, Montreal, Canada; Leonides Andreu Almazan, chief, department of health, Mexico, and Edwin H. Schorer, Kansas City. The 1939 meeting will be in Pittsburgh.——Dr. Louis L. Williams Jr., U. S. Public Health Service, Washington, D. C., was chosen president-elect of the American Society of Tropical Medicine at the annual meeting in Oklahoma City November 15-18. Dr. Alfred C. Reed, San Francisco, became president; Drs. Sterling S. Cook, Portsmouth, Va., and E. Harold Hinman, Wilson Dam, Ala., were elected vice president and secretary respectively.——Dr. James K. McGregor, Hamilton, Ont., was chosen president-elect of the American Association for the Study of Goiter at the recent annual meeting during the International Goiter Conference in Washington, D. C. Dr. Frank B. Dorsey Jr., Keokuk, Iowa, became president and Dr. Claude J. Hunt, Kansas City, was elected vice president. Dr. William Blair Mosser, Kane, Pa., is corresponding secretary and Dr. George C. Shivers, Colorado Springs, recording secretary.——Dr. Paul A. O'Leary, Rochester, Minn., was elected president of the American Academy of Dermatology and Syphilology at the annual meeting in St. Louis in November. Dr. Harther L. Keim, Detroit, was elected vice president and Dr. Earl D. Osborne, Buffalo, secretary. The 1939 meeting will be held in Philadelphia.

Fellowships in Medical Sciences.—The National Research Council announces that the following fellows, appointed by the medical fellowship board, have begun their work:

Dr. Louis K. Alpert, Chicago, at the Rockefeller Institute for Medical Research, New York.
Philip P. Cohen, Ph.D., Madison, Wis., at the University of Sheffield, England.
Thomas H. Davies, Ph.D., Baltimore, at the California Institute of Technology, Pasadena.
Dr. Carl L. Larson, Butte, Mont., at the University of Rochester (N. Y.).
Dr. Arthur P. Richardson, San Francisco, at John Hopkins University, Baltimore.
Jane A. Russell, Ph.D., Berkeley, Calif., at Yale University, New Haven, Conn.
Wilfred W. Westerfeld, Ph.D., St. Louis, at Oxford University, Oxford, England.

Symposium on Mental Health.—The section on medical sciences of the American Association for the Advancement of Science will conduct a symposium on mental health at the annual Christmas meeting in Richmond, Va., December 28-30. Sessions will be held at the Commonwealth Club except the final general session, which will be at the Mosque. Contributions to the symposium will be printed in advance and the sessions will be devoted to discussion of them. One topic will be discussed at each session. Dr. Charles Macfie Campbell, professor of psychiatry, Harvard University Medical School, Boston, will give the summary and address at the general session. Among the contributions listed in the program are:

Dr. Charles P. Fitzpatrick, Providence, R. I., Facilities for Research.
E. Morton Jellinek, M.Ed., Worcester, Mass., Function of Biometric Methodology in Psychiatric Research.
Dr. George Gilbert Smith, Boston, Relationship of Birth Control to Mental Conditions.
Dr. John D. Reichard, Ellis Island, N. Y., Immigration and the Mental Health of Communities.
Carney Landis, Ph.D., New York, and James Page, Ph.D., Rochester, N. Y., Magnitude of the Problem of Mental Disease.
Dr. Helen Flanders Dunbar, New York, Bearing of Emotional Factors on Social-Health Programs Dealing with Economic Disability.
Edward Sapir, Ph.D., New Haven, Conn., Psychiatric and Cultural Pitfalls in the Business of Getting a Living.
Charles C. Limburg, Ph.D., Lexington, Ky., Community Differences and Mental Health.
Dr. Winfred Overholser, Washington, D. C., Psychiatric Expert Testimony.
Dr. George S. Stevenson, New York, Psychiatry in a Community.
Dr. Edward A. Strecker, Philadelphia, Undergraduate Instruction in Psychiatry in the United States and Canada.

Dr. Thomas M. Rivers, New York, is chairman of the section on medical sciences and Malcolm H. Soule, Sc.D., Ann Arbor, Mich., is secretary. Dr. Walter L. Treadway of the U. S. Public Health Service, Lexington, Ky., is chairman of the program committee.

Government Services

Government Dedicates Narcotic Hospital at Fort Worth

The U. S. Public Health Service hospital for narcotic addicts at Fort Worth, Texas, the second of its type, was dedicated October 28. Dr. Thomas Parran, surgeon general, U. S. Public Health Service, made the dedicatory address and other speakers were Dr. Lawrence Kolb, assistant surgeon general in charge of the division of mental hygiene of the public health service, and James V. Bennett, director of the bureau of prisons of the department of justice. The new institution covers 1,400 acres and cost $4,000,000. It includes an administration building, a clinical ward building, a maximum custody ward, residences for personnel and maintenance structures. A prolonged treatment building for advanced cases of addiction will be ready in 1939. The first narcotic hospital at Lexington, Ky., was opened in 1935. It is said that the Fort Worth unit places less emphasis on custodial features, such as bars, high gates and walls and inclosed courts. Passed Assistant Surgeon William F. Ossenfort of the service, medical director of the new hospital, is a graduate of Washington University School of Medicine, St. Louis.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 12, 1938.

Cardio-Omentopexy

The important advance of Mr. Laurence O'Shaughnessy in introducing the operation of cardio-omentopexy to provide collateral circulation in cases of cardiac ischemia, with its resultant angina pectoris, has been described in previous letters. The report of the Royal College of Surgeons for 1937-1938 contains a note on the experimental and clinical work performed by him during the year in conjunction with Dr. Slome, on which they have a paper in preparation. They have demonstrated that vascular continuity between a graft and the coronary tree can be obtained without the use of myocardial sutures, provided a special aleuronat preparation is used. Early experiences with the danger and difficulty of inserting stitches into a friable and degenerated myocardium make this an important technical advance. They have also shown that a graft applied to an adherent pericardium can still be effective. The importance of this observation was emphasized at a recent operation when they encountered pericardial adhesions at the site of a fairly recent infarct. Some of the experiments of Lezius, who first showed that the lung can rapidly form vascular adhesions with the heart after incision of the parietal pericardium, were repeated and his results confirmed.

The electrocardiogram of the grafted heart shows specific changes. Mr. O'Shaughnessy and Dr. Slome have records collected from several patients over a period of a year and more. An attempt to correlate their observations with electrocardiograms of grafted animals is still in progress. They have found that acute coronary occlusion may complicate the results of operation, and an experimental investigation of its treatment has become pressing.

The results in a series of twenty patients with cardiac ischemia operated on in the Lambeth cardiovascular clinic were published early in 1938. The survivors in this series and of more recent operations are still under observation. Patients who have survived the operation for one year and in some cases for two years continue to be active. One death from heart failure has occurred in the group, and if deaths from heart failure continue to be rare or absent as the group becomes larger, this fact alone will be significant.

Casualties of Air Raids

Speaking at the council dinner of the British Medical Association, the Right Hon. Walter Elliot, minister of health, said that on June 1 he took over the responsibility of organizing the emergency hospital system against the possibility of air raids. A survey had already been made of 3,000 hospitals and institutions and 400,000 beds. Hospital officers were appointed in every region of the country except London and asked to prepare schemes for the best utilization of hospital accommodation. At the same time a committee of medical experts presided over by Sir Charles Wilson, dean of St. Mary's Hospital, was appointed to consider the provision for London casualties, the type of hospital to be utilized for them and the extent to which peace time patients could be moved. In early August contact was established with every hospital throughout the country and they were asked to clear as many beds as possible on receiving warning from the government that an emergency had arisen. In September the international situation was so acute that plans had to be concentrated for immediate operation. Large orders were placed for hospital requirements, including surgical equipment for hospitals not then capable of dealing with casualties. On the last day of August every hospital officer was given instructions to accelerate plans for clearing hospital beds, and 150,000 beds, with medical attendance and nursing complete, would have been available within twenty-four hours. That was only the beginning. Representatives of thirty-four of the larger London hospitals to be evacuated and representatives from the receiving areas were received by the ministry. Ambulances, both train and automobile, were organized. By September 24 the necessary number of stretchers were distributed to each hospital. From that moment the hospital evacuation scheme could have been put into operation within twenty-four hours of the warning. The crisis passed, but that was not the end of the possible emergencies. The hospitals were now being registered where surgical facilities could be improved.

PARIS

(From Our Regular Correspondent)

Nov. 12, 1938.

Paris Physicians Protest Against Social Insurance

The abuse of free medical care by the public hospitals and dispensaries and the illegal extension of the original function of the social insurance authorities are arousing the French medical profession to make a vigorous campaign to put an end to a movement which renders it difficult for physicians to earn a living. In the notice sent out by the association of physicians in the department of the Seine, in which Paris is situated, for a meeting to be held Nov. 4, 1938, the following plea was made for a full attendance:

1. It is becoming more and more difficult, in fact almost impossible, to practice in Paris and the adjacent areas.

2. The public hospitals and dispensaries, which are not subjected to the excessively high taxes which physicians must pay, are doing all they can to give free medical attention without any inquiry as to the ability of the sick to pay. Such institutions should treat only indigents.

3. The social insurance organization was created to insure the worker earning up to a certain sum annually, now 30,000 francs, so that he might be able to pay for medical care. Instead of limiting their activities to this commendable objective, the social insurance authorities have begun to make serious inroads on the work of private practitioners by attempting to organize facilities for treating the insured worker. Every effort is being made to turn the insured from specialists and general practitioners by urging them to enter public hospitals or receive treatment at the many public dispensaries.

4. The situation has become so acute that the time has arrived for a more energetic campaign against these abuses, which make it impossible for a physician, after many years of preparation, to compete with the tendency toward state medicine.

Foreign Physicians Being Naturalized in France

Not only is there a marked increase in the number of first year medical students at all the medical schools here, but there is a fear that the government is giving permission to become naturalized to more physicians coming to France than there is room for in the profession. The number of foreign physicians who wish to practice here rose from four in 1935 to ninety-four in 1937. The Armbruster law, passed in 1933, requires all physicians of foreign birth not only to be naturalized but to serve the same length of time in the army or navy as those born in France or its colonies. At a recent meeting of the association which has charge of public relations for the French medical profession, the secretary, Dr. Cibrie, stated that permission to become naturalized is being too easily granted by the authorities, without adequate investigation of the past records of the applicants. An information bureau has been opened by the Confederation of Medical Syndicates, as the central organization is termed, to furnish the authorities with all data as to whether or not an applicant for naturalization is worthy of remaining in France.

Antitoxin-Toxoid Treatment of Diphtheria and Tetanus

The question of whether the transitory passive immunity following the injection of diphtheria or tetanus antitoxin can be converted into a more permanent active immunity by simultaneous use of the diphtheria or tetanus toxoid has been the subject of papers at recent meetings of the Société médicale des hôpitaux of Paris. At the July 22 meeting the results of the combined use of the diphtheria antitoxin and the toxin were reported from three Paris hospitals. In the first paper Drs. René Martin and his co-workers stated that they had given the treatment to twelve children with diphtheria. A subcutaneous injection of 0.1 cc. of the toxoid was followed twenty minutes later by a single large dose of antitoxin. Forty-eight hours later a second injection, varying from 0.3 to 0.5 cc. of the toxoid, was given. Subsequently the toxoid in gradually increasing doses, beginning with 1 cc., was given every five days. Aside from slight febrile and local reactions after the first and second injections of the toxoid, no ill effects were noted. These reactions seem to be of an antigenic and not of an allergic character.

The titer of the antitoxin in the blood was measured at frequent intervals after the first injection of the toxoid. These determinations showed that the passive immunity conferred by the antitoxin does not interfere with the development by the toxoid of an active immunity in the majority of cases. Patients who had a well marked incipient immunity before the antitoxin was given showed a striking rise in the titer of the antitoxin in the blood after injection of the toxoid. Patients who failed to show any antidiphtheria immunity before being given the antitoxin showed a distinct but less marked increase in the titer of the antitoxin in the blood after injection of the toxoid. These observations appear to confirm the theory of Prof. Gaston Ramon that the brief transitory passive immunity conferred by the diphtheria antitoxin is succeeded by an active immunity which is more stable and of longer duration when the toxoid also is given.

OBSERVATIONS ON SOLDIERS

In a second paper, Drs. Sohier and Jaulmes reported their observations on eleven soldiers with diphtheria at the large Val-de-Grace Hospital. A diphtheria toxoid with a titer of 150 units per cubic centimeter was used. A dose of 0.1 cc. was given the first day and was followed one hour later by a massive single dose of diphtheria antitoxin. This was followed by the injection at regular intervals during the remainder of the hospitalization of gradually increasing doses of the diphtheria toxoid. The eleven patients all recovered, no reaction of any importance following the use of the diphtheria toxoid being noted. Estimations of the titer of diphtheria antitoxin in the blood serum of the eleven patients were made over a period of six months. These estimations showed the constant presence of a titer of antitoxin in the blood serum adequate to protect the patient against a recurrence of the infection. This observation shows the advantage of the use of Ramon's combined antitoxin and toxoid administration as applied to a collectivity such as an army.

OBSERVATIONS ON CHILDREN

In a third paper, Drs. Darré and Lafaille reported their results with thirty-three children who had diphtheria. Of these, four had a malignant type, four had a severe form and sixteen had moderately severe form. In the last-named group, although some were not seen until the third or fourth day, no paralysis of the soft palate followed. In the seven with severe involvement, in spite of extensive formation of false membrane, no complications were noted. In all four with the malignant type an early paralysis of the soft palate was observed but there were no other sequels, such as generalized paralysis or cardiac and respiratory symptoms. These four children all recovered, although in one the prognosis appeared very unfavorable. There were no deaths in the other twenty-nine cases.

The mode of administration in the thirty-three cases was as follows: On admission the child was given an injection in the left subscapular region of 0.1 cc. of a purified diphtheria toxoid with a titer of 150 units to the cubic centimeter. A half hour later a single massive dose of antitoxin, varying from 18,000 to 40,000 units according to the severity of the attack, was injected in the abdominal region. Forty-eight hours later, 0.5 cc. of the toxoid was injected, and then at intervals of five days two injections of toxoid, 1 cc. and 2 cc. respectively, were given. Before every injection the titer of antitoxin in the blood serum was determined, and it showed results which agreed with those of the observers cited.

In the discussion of these papers Dr. Marquezy failed to share the enthusiasm which the others had expressed regarding this new treatment of diphtheria. The number of patients thus far treated is too small to permit definite conclusions to be drawn. At present he believed that the antitoxin-toxoid treatment greatly complicated matters.

Brucellosis Congress

The subject selected by the Federation of Medical Societies of Northern Africa for its next congress is brucellosis. The meeting will be held at Oran, Algeria, in April 1939. The titles of the papers to be read are epidemiology of the brucelloses, bacteriologic identification, clinical forms, medical and surgical complications, treatment, animal brucelloses and prophylaxis in Tunis, Algeria and Morocco. Those wishing to attend the congress are asked to write to Dr. René Solal, 16 Boulevard Joffre, Oran, Algeria.

Many Physicians in French Parliament

There are a relatively large number of physicians in both the Chamber of Deputies and the Senate. At a recent election for senators in thirty departments, twelve physicians were elected or reelected. Many important laws affecting the medical profession have had their origin in bills submitted by physicians who were deputies or senators.

Death of Proctologist

Many American proctologists have visited the clinics of Dr. Raoul Bensaude of Paris, who died during October. His book on rectosigmoidoscopy is used all over the world, and before his death he had just completed the fourth volume of a series on diseases of the intestine.

BERLIN

(From Our Regular Correspondent)

Nov. 1, 1938.

Genealogic Survey of the German People

A new comprehensive type of genealogic survey based on previous investigation has been ordered by the minister. This survey is basically intended to include the entire population, although it will at first concern itself with those groups among which eugenic and racial hygienic measures have been or are being carried on according to recognized legal stipulations. The new survey will represent in general an assembly of all data which may be relevant to the evaluation of the eugenic and racial status of familial groups and their members. Health officials record the data with regard to individual persons in a genealogic card catalogue and the data on familial groups in a special registry. The registration place for each person is the health bureau having jurisdiction over his place of birth. A table of the familial group has been devised which forms the matrix of a genealogic axis about which all particular data with regard to a group are assembled. Such a table is created for each family. The sum of familial data go to make up the registers of familial groups. The tables are to be compiled for as great a number of families as possible in order to promote the genealogic survey of the entire population.

New Regulations for Nursing

The national government has just issued a "Statute for Regulation of Nursing," which contains certain innovations. In Germany, as elsewhere, a crisis in nursing has long existed. This crisis, according to a statement emanating from professional sources, expresses itself most clearly in a lack of a new generation of persons willing to enter Christian nursing orders. This state of affairs has been exacerbated by the spiritual degeneration incident to the Nazi revolution. The acute shortage of younger persons in the religious nursing organizations has been paralleled by a stronger influx into the Nazi Sisterhood as well as into the German Red Cross, the latter group having been reorganized along Nazi lines. Nevertheless, the need for a greater number of younger nurses is still urgent; the number of training schools is likewise inadequate. These circumstances underlie promulgation of the new decree, which now, for the first time, envisages a nationwide regulation of the nursing profession. Public hospitals are now compelled to establish and maintain nurses' training schools either at their own expense or, if necessity requires, with the aid of public funds. These schools must enroll the young apprentice sisters according to the maximal quotas prescribed by law for each institution. The training of male nurses is similarly regulated. The director of a nurses' training school must be a physician and the assistant director either a nursing sister or a male nurse. These officers must be morally and politically reliable (Nazi style) as well as of German blood. Like qualifications are demanded of matriculants in the nursing schools. Hereafter the course of training will cover only one and one-half years, instead of two years, as formerly. Professional training must be predominantly practical; the theoretical courses must be in part conducted by physicians. An official handbook serves as the basis of instruction. The curriculum must include an introduction to "weltanschaulichen," ethical principles of the nursing profession and, besides, regular classes in bodily hygiene. Compulsory insurance against personal injury and sickness is stipulated. Since October 1 only persons who hold special official licenses have been permitted to practice the nursing profession. The license is issued to a person who has passed the examination, but at first the nursing activities of the graduate are restricted to a public hospital. Only after a year of nursing in such an institution is the licensee certified for nursing outside a public hospital. A license may be revoked if the essential prerequisites of its granting become nullified, for example on the basis of political and moral unreliability, bodily or mental handicap or addiction to alcohol or narcotic drugs. Jews may practice nursing only among other Jews and in Jewish hospitals. Jewish nurses can receive training only in Jewish schools.

The new law represents a great improvement over the previous situation, in which the practice of the nursing profession was open to all and without government recognition.

Psoriasis

Julius Mayr, professor of dermatology at Munich, has published a study of the problem of the heritability of psoriasis vulgaris. The author found analogous cases in a pair of enzygotic female twins. It is significant that the disease was manifested earlier and assumed a severer form in the twin whose bodily weight was the greater. From study of a family tree which comprised records of fifty-eight members over four generations, it was ascertained that psoriasis had been present in the generation of the grandparents but had reappeared only in the twins (four siblings of the latter were unaffected). The parent generation exhibited no signs of psoriasis. Also from the genealogic table it was ascertained that the penetrating power of psoriasis is often extremely slight, since the disease was found to be much less extensively distributed than would have been the case in a dominant hereditary transmission. It appears noteworthy that in this family diabetes was present in three members on the same (maternal) side.

Prof. Karl Sudhoff Is Dead

Prof. Karl Sudhoff, former ordinarius of the history of medicine at Leipzig University, died shortly before completion of his eighty-fifth year. A country practitioner for some thirty years, Sudhoff in 1905 left the small town in which he had worked to accept appointment as extraordinarius in the newly founded chair of medical history at Leipzig. This chair was the first of its kind in Germany. Sudhoff's publications on medical history attracted widespread attention. While engaged in general practice, he had earned a notable reputation as a Paracelsus scholar. At Leipzig he grew to be the leading medical historian. His research on manuscripts represented surprisingly rich contributions to our knowledge of medieval medicine. In 1903, in collaboration with the chemist Kahlbaum, Sudhoff founded the German Society of Medical and Natural Scientific History. At Leipzig he established and headed the first regular Institute of Medical History. In the following decades Sudhoff's activities, and especially his writings, brought modern medicohistorical research into high regard. Worthy of note in addition to the mentioned paracelsian studies is Sudhoff's pioneer work in medieval balneology and the history of syphilis. The guiding principle of Sudhoff's thought was constantly to serve the present by study of the past. In 1919 he became ordinarius and his retirement took place in 1925. Later, after his successor, Prof. H. E. Sigerist, had quit Leipzig for Baltimore, Sudhoff resumed professorial activity and directorship of the institute. His eightieth birthday found him still vigorously active in this capacity. Sudhoff was greatly honored for his services. Among other things he was doctor honoris causa of philosophy and veterinary medicine and honorary member of the Royal Society of Medicine of London and of the Society of Medical History of Chicago. The German Society of Medical History changed its style to "Sudhoff-Gesellschaft" in his honor. Sudhoff was the extremely active editor of "Classics of Medicine," "Studies in Medical History" and the journal *Archiv für Geschichte der Medizin*, among other publications.

NETHERLANDS

(From Our Regular Correspondent)

Oct. 8, 1938.

The Institute of Thermology

The Warmte Stichting (institute of thermology) foundation has commemorated its tenth anniversary. This foundation, in addition to its usual function of inspection, has examined such problems as desiccation of grain, the ventilation of stables, the radiation of hearths and stoves, the conduction of heat in building materials and buildings, and central heating. New methods of measurement have been developed by the institute; among others a method for gaging the ventilation of dwelling rooms and work rooms, and a thermo-electric instrument for measurement of humidity. The foundation's chief of technical service took an active part in the work of the commission appointed to study atmospheric conditions in the buildings constructed by the Royal Institute of Engineers.

Combined Immunization Against Scarlatina and Diphtheria

In North Holland province, since 1930, tens of thousands of children have submitted to combined immunization against scarlatina and diphtheria, effected by a mixture of diphtheria antitoxin and scarlatina antitoxin. This immunization has favorably influenced the incidence of diphtheria and also, to a lesser degree, the incidence of scarlatina. In 1937, among 25,018 inoculated children from 6 to 13 years of age, the scarlatina morbidity was 15.1 : 10,000; among 29,127 children not immunized the rate was 50.1 : 10,000. Inoculation did not cause any serious complications, although local reactions occurred sometimes accompanied by a scarlatiniform exanthem and slight elevation of temperature.

JAPAN

(From Our Regular Correspondent)

Oct. 29, 1938.

Air Raid Experiment in a Basement

For the protection of air raid refugees, the Industrial Hygiene Society, the planning board of the home office and the city protection association at Kanda joined September 12 in making a three hour experiment in the basement of the Hundredth Bank in the middle of Tokyo. Seventy adults participated, including forty-two examiners and inspectors. The directors were Shigeyuki Kitaura and Kentaro Kuroyanagi, engineers. The department of architecture and the sanitation department of the Tokyo Imperial University participated. The army and the navy sent its inspectors. The aim was to observe the ventilation when many refugees were shut up in a closed place and to learn how long they could remain. The basement was provided with every protection against poison gas, and every crevice was sealed up with gum tape. The twenty-eight examinees, of whom the oldest was 64 and the youngest 18, were all male. After a physical examination they went down into the basement. They wrote down on cards at any time they wanted what they felt and thought. The room was 25 square meters in area and 2.6 meters in height. As the examinees were closely packed in this room the temperature and humidity were reported every half hour to the office on the first floor. At 1:35 p. m. the temperature was 28.1 C. (82.5 F.) and the humidity 86, but they both gradually rose, and at 4:35 the former was 32.6 C. (90.7 F.) and the latter 99. At 4:18 a man of 48 found that he was unable to remain, while all the rest stood firm for the three hours without any notable ill effects. Further stay was thought to be dangerous. Detailed reports are to be made public in the near future.

Military Medicine

Surgeon Major General Koizumi, chief of the bureau of military medicine, made a report on recent progress at a meeting of the Kyushu Medical Society. He defined military medicine in its broad sense as quite different from the military medicine based on fighting, or individual treatment. Medicine which aims to treat individuals has checked the progress and development of military medicine. In its broad sense military medicine requires public health establishments, social supplementary training and suitable surroundings for every profession and business. Universal strengthening of the nation's health ought to be considered. In the narrow sense, military medicine aims to strengthen the soldier's physical constitution. Medicine ought not to confine itself within its old circles but should dare to embrace researches into the social life. The speaker went on to the problem of how to have better efficiency in fighting, how to obtain a large quantity of pure water to supply soldiers, how to provide soldiers with ample food in the field and how to reeducate the wounded to furnish them with new occupations. He added that in the past war the number of the ill at the front was three or four to one wounded in fighting, but that in the present war the number has been reduced to 1.5 with illness to one wounded. This fact shows the development of military medicine.

Reopening of Peking University

The old Peking University in North China was compelled to close because of the war between China and Japan. It is now making preparations for resuming lectures, and a great change in the organization is going to be realized with aid from Japan. The medical department, which was opened recently, has as its dean Prof. Dr. Hisomu Nagai, who had been dean in the Formosa Medical College after retirement from Tokyo Imperial University, and twelve professors and assistant professors, all Japanese, have been appointed. The agricultural department was opened in September with many Japanese professors. An engineering department will be attached to the university, also with many Japanese on its staff. The total number of Japanese professors is estimated to be over sixty. The course is to be four years, and postgraduate courses will be founded to train graduates who wish to be specialists.

All Medical Men Must Register

The government has enacted a new law for the registration of persons who are connected with medicine. The law requires reports from every physician, dentist, pharmacist and nurse who lives in Japan or in its territory abroad, including the South Sea islands. Once in every four years, on August 1, such persons are obliged to present a report concerning their ability to serve the government. Those who fail to make returns are liable to a penalty of 500 yen ($135). Some of the chief articles in the report concern military service, condition of health, possibility of engaging in the national mobilization and family relations. About 59,700 physicians, 21,000 dentists, 26,700 chemists and 110,000 nurses are expected to make reports.

Dr. Irisawa Is Dead

Dr. Tatsukichi Irisawa, honorary professor of Tokyo Imperial University, died at the age of 74 at the university hospital of pyelitis. After graduating in 1889 he was sent by the government to Germany to study for several years. In 1902 he was appointed to the chair of internal medicine. In 1921 he was made dean of the medical department and at the same time was appointed chief of court physicians. He held the latter position until 1927, when he resigned. In his will he asked his followers to dissect his body. He especially requested that his brain be dissected, for he had suffered from infantile paralysis at the age of 2.

Marriages

Martin A. Compton, 1st Lieut., M. C., U. S. Army, Fort Benjamin Harrison, Ind., to Miss Bertha Mae La Fara of North Vernon, October 22.

Donald T. Hughson, Madison, Conn., to Dr. Frances Kathryn Gramling of Milwaukee, September 28.

William C. Sheehan, Stevens Point, Wis., to Miss Antoinette M. Doolan of Madison, October 22.

Maurice A. F. Hardgrove, Milwaukee, to Miss Olive Van Susteren of Little Chute, Wis., September 3.

Arthur L. Reinardy, Stevens Point, Wis., to Miss Helen Steingraeber of Kewaunee, September 17.

John P. Harney, Hartsdale, N. Y., to Miss Phyllis M. Hannemann of New York, August 6.

Otto E. Toenhart, Sheboygan, Wis., to Miss Bessie McIntyre of Madison, September 17.

Alberti Fraser Lapsley, Badin, N. C., to Miss Mary Jane Hall of Roanoke, Va., November 12.

Howard J. Laney, Prescott, Wis., to Miss Katherine V. May of Madison in September.

Eugene E. Burzynski, Laona, Wis., to Miss Helen Krieger of Milwaukee, September 30.

Thomas Paine Saltiel, Chicago, to Miss Gene Sternberg of New York, November 14.

Harold L. Miller to Miss Margaret Marian Plonsker, both of Milwaukee, August 10.

Myron T. McCormack to Miss Edna Lucille Purtell, both of Milwaukee, September 3.

Charles Quirico de Luca to Miss Cecilia McCarthy, both of Philadelphia, October 29.

Leo A. Jordan to Miss Adrienne L. Bates, both of Saginaw, Mich., September 22.

Harvey G. E. Mallow to Miss Alice Dierker, both of Watertown, Wis., July 21.

Hugh A. Cunningham to Miss Mildred Owen, both of Milwaukee, August 28.

Frank A. Majka to Miss Ruth N. Ryan, both of Pueblo, Colo., October 24.

William F. Ragan, Milwaukee, to Miss Myrtle Halverson, September 24.

Deaths

Addinell Hewson ● Philadelphia; Jefferson Medical College of Philadelphia, 1879; emeritus professor of anatomy, Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; formerly professor of anatomy and histology at Temple University School of Medicine; at various times assistant professor of anatomy and demonstrator at his alma mater; fellow of the American College of Surgeons and member of the American Association of Anatomists; served on the staff of the Episcopal Hospital, where he was dispensary surgeon from 1887 to 1904; surgeon to St. Timothy's Hospital, now known as the Memorial Hospital, from 1894 to 1928; aged 83; died, October 27, at his home in Bryn Mawr, Pa.

Leo Melville Crafts ● Minneapolis; Harvard University Medical School, Boston, 1890; an Affiliate Fellow of the American Medical Association; professor of nervous and mental diseases, Medical Department of Hamline University, 1893-1908, and dean, 1897-1903; past president of the Minnesota Neurological Society; served during the World War; delegate to the International Congress of Medicine, London, 1913, and the International Neurological Congress, Berne, Switzerland, 1931; on the staffs of the Minneapolis General, St. Mary's, St. Barnabas, Asbury, Swedish, Eitel and Maternity hospitals; aged 74; died, September 22, of coronary thrombosis.

Frank Sidle Lynn ● Baltimore; University of Maryland School of Medicine, Baltimore, 1907; professor of clinical surgery at his alma mater; member of the American Surgical Association and the Southern Surgical Association; formerly vice president of the Medical and Chirurgical Faculty of Maryland; fellow of the American College of Surgeons; visiting surgeon to the University, Mercy, Franklin Square and Bon Secours hospitals, Hospital for Women of Maryland and Baltimore City Hospitals; aged 54; died, September 26, of cerebral hemorrhage.

John Clement Heisler ● Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1887; since 1930 emeritus professor of anatomy at his alma mater and professor of anatomy, 1916-1930; professor of anatomy at the Medico-Chirurgical College of Philadelphia, 1898-1916; member of the American Association of Anatomists; author of "Textbook of Embryology," 1898, 1901 and 1907, and "Textbook of Practical Anatomy," 1912; aged 76; died, September 9, of chronic myocarditis.

John Bruce McCreary, Shippensburg, Pa.; University of Maryland School of Medicine, Baltimore, 1892; member of the Medical Society of the State of Pennsylvania; formerly deputy secretary of health for Pennsylvania and chief of the bureau of child health; served during the World War; past president of the American Association of School Physicians; on the staff of the Chambersburg (Pa.) Hospital; aged 68; died, September 13, of coronary embolism.

John Martin Julius Raunick, Harrisburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; member of the Medical Society of the State of Pennsylvania; health officer; past president of the Dauphin County Medical Society; past president of the Harrisburg Academy of Medicine; formerly on the staff of the Harrisburg Hospital; aged 63; died, September 15, of arteriosclerosis.

William Woodburn ● Boone, Iowa; Hahnemann Medical College and Hospital, Chicago, 1888; past president and secretary of the Boone County Medical Society; health officer; president of the Iowa Public Health Association; on the staff of the Boone County Hospital; aged 78; died, September 2, of cerebral hemorrhage with right hemiplegia.

Myers Worman Horner, Mount Pleasant, Pa.; Jefferson Medical College of Philadelphia, 1896; past president and secretary of the Westmoreland County Medical Society; formerly deputy coroner; at one time member of the school board; on the staff of the Henry Clay Frick Memorial Hospital; aged 67; died, September 26, of multiple neuritis.

Willard Henry Pierce, Greenfield, Mass.; University of Vermont College of Medicine, Burlington, 1885; member of the Massachusetts Medical Society; formerly on the staff of the Franklin County Public Hospital; aged 72; died, September 24, in Montague of chronic myocarditis, empyema and bronchopneumonia.

Frank Winfield Laidlaw ● Middletown, N. Y.; Jefferson Medical College of Philadelphia, 1903; district health officer; member of the consultant staffs of the Horton Memorial Hospital, Middletown, Monticello (N. Y.) Hospital and the Maimonides Hospital, Liberty; aged 62; died, September 20.

Isaac N. McComb, Brillion, Wis.; Chicago Medical College, 1877; member of the State Medical Society of Wisconsin; health officer in Brillion for many years and on numerous village and county boards; formerly member of the state legislature; aged 87; died, September 27, of arteriosclerosis.

George Erastus Goodrich ● Phoenix, Ariz.; Rush Medical College, Chicago, 1906; fellow of the American College of Surgeons; on the staffs of St. Joseph's and Good Samaritan hospitals; surgeon to St. Luke's Hospital; aged 59; died, September 3, in Los Angeles of heart disease.

Lawrence Ewald Lepper ● Los Angeles; University of California Medical Department, San Francisco, 1912; fellow of the American College of Surgeons; served during the World War; on the staff of the California Hospital; aged 51; died, September 18, of heart disease.

Albert George Gorczyca ● Elizabeth, N. J.; Georgetown University School of Medicine, Washington, D. C., 1929; aged 32; on the staffs of the Alexian Brothers Hospital and St. Elizabeth Hospital, where he died, September 24, of hypertrophic cirrhosis of the liver.

Frank Robert Smith Sr., Baltimore; University of Maryland School of Medicine, Baltimore, 1891; member of the Medical and Chirurgical Faculty of Maryland; formerly associate of medicine, Johns Hopkins University; aged 82; died, September 26, of heart disease.

Raynauld Dobson Richman ● Hartford, Conn.; University of Buffalo School of Medicine, 1908; served in the World War; for many years connected with the Aetna Life Insurance Company; aged 53; died, September 16, of hypertensive cardiovascular renal disease.

Kennard J. French, Factoryville, Pa.; Kentucky School of Medicine, Louisville, 1905; member of the Medical Society of the State of Pennsylvania; aged 75; died, September 26, in the Moses Taylor Hospital, Scranton, of arteriosclerosis and hypostatic pneumonia.

Robert Alexander Simpson, Washington, Ga.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1884; member of the Medical Association of Georgia; aged 79; died, September 24, of carcinoma of the prostate.

Elmer Hinckley Heath ● Buffalo; Harvard University Medical School, Boston, 1923; assistant dean and associate professor of medicine, University of Buffalo School of Medicine; aged 43; died, September 23, of hypertension and arteriosclerosis.

Benjamin M. Watkins ● Derry, Pa.; Jefferson Medical College of Philadelphia, 1909; bank president; aged 54; on the staff of the Latrobe (Pa.) Hospital, where he died, September 30, of pulmonary embolism following injuries received in a fall.

Cloud M. Jackson, Elizabethtown, Ind.; Hospital College of Medicine, Louisville, 1903; member of the Indiana State Medical Association; served during the World War; formerly county coroner; aged 61; died, September 29, of myocarditis.

Robert Lee Friabie ● Rhinelander, Wis.; Marion-Sims College of Medicine, St. Louis, 1894; for many years deputy state health officer; aged 68; died, September 17, in the Wisconsin General Hospital, Madison, of cerebral arteriosclerosis.

Ray H. Johnson ● Buffalo; University of Buffalo School of Medicine, 1893; fellow of the American College of Surgeons; aged 70; on the staff of the Deaconess Hospital, where he died, September 17, of fracture of the skull resulting from a fall.

James Aubrey Lippincott, Nice, France; Jefferson Medical College of Philadelphia, 1873; member of the Medical Society of the State of Pennsylvania and the American Ophthalmological Society; aged 91; died, September 23.

Frank George Ungerman ● McKeesport, Pa.; University of Louisville (Ky.) Medical Department, 1912; aged 50; on the staff of the McKeesport Hospital, where he died, September 26, of cerebral hemorrhage and chronic nephritis.

John W. Bachelor, Oxford, Mich.; Detroit College of Medicine, 1897; member of the Michigan State Medical Society; served during the World War; aged 63; died, September 23, of carcinoma of the stomach with metastasis.

John Warren Germany, Ennis, Texas; Kentucky School of Medicine, Louisville, 1890; served during the World War; formerly on the staff of the Municipal Hospital; aged 71; died, September 23, of coronary thrombosis.

Joseph Welch Scott, West Point, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1887; member of the State Medical Association of Texas; aged 74; died, September 11, at the Ivy Hospital.

Robert Burtis Blanchard ● Jamestown, N. Y.; University of Buffalo School of Medicine, 1906; aged 55; on the staff of the

Jamestown General Hospital and the Woman's Christian Association Hospital, where he died, September 15.

Frank Mansfield Sharpe, Oconomowoc, Wis.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1887; aged 75; died, September 13, of chronic myocarditis and arteriosclerosis.

Samuel Beecher Pray ● New Rochelle, N. Y.; University and Bellevue Hospital Medical College, New York, 1901; on the staff of the New Rochelle Hospital; aged 65; died, September 7, in the Glens Falls (N. Y.) Hospital.

William Walter Pretts ● Milwaukee; Northwestern University Medical School, Chicago, 1900; served during the World War; on the staff of the Veterans Administration Facility; aged 65; died, September 7, of heart disease.

Alfred Elias Orr, Montreal, Que., Canada; McGill University Faculty of Medicine, Montreal, 1888; at one time lecturer in anatomy and demonstrator of biology at his alma mater; aged 77; died, September 23.

John Bernhard Thompson, Wittenberg, Wis.; Milwaukee Medical College, 1912; served during the World War; aged 51; died, September 6, in the Memorial Hospital, Antigo, of peritonitis and ruptured gallbladder.

Arthur Franklin Gerberich, Limeport, Pa.; Medico-Chirurgical College of Philadelphia, 1909; member of the Medical Society of the State of Pennsylvania; aged 52; died, September 21, of pulmonary carcinoma.

Aloys Heinen, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; aged 76; died in September in Germany of chronic myocarditis and arteriosclerosis.

James W. Ludden, Cincinnati; University of the South Medical Department, Sewanee, Tenn., 1894; aged 75; died, September 28, in St. Agnes Hospital, Philadelphia, of hypostatic pneumonia and arteriosclerosis.

Thomas Richmond, Guthriesville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1881; member of the Medical Society of the State of Pennsylvania; aged 81; died, September 2, of uremia.

Peter Lorentz Vistaunet, Thief River Falls, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; aged 67; died, September 22, of bronchopneumonia and myocardial insufficiency.

Jacob B. Oliver, Brazil, Ind. (licensed in Indiana in 1897); formerly a medical missionary and minister; aged 91; died, September 21, of carcinoma of the right cheek and jaw and bronchopneumonia.

Philip Arlis Hilton, Waynesboro, Va.; Howard University College of Medicine, Washington, D. C., 1920; aged 49; died, September 25, in the University Hospital, Charlottesville, of bronchopneumonia.

Willard Hanks Gage, Seattle; Eclectic Medical Institute, Cincinnati, 1899; aged 60; died, September 16, of injuries received in an automobile accident in the mountains near Jackson, N. Y.

Harry Melville Dougherty ● Pittsburgh; University of Pittsburgh School of Medicine, 1925; served during the World War; aged 41; died, September 13, of pulmonary tuberculosis.

John Walton Shultz, Kansas City, Mo.; University Medical College of Kansas City, Mo., 1902; aged 79; died, September 16, of chronic myocarditis, cystitis and arteriosclerotic nephritis.

John Peyton Foster, La Crosse, Mo.; Marion-Sims College of Medicine, St. Louis, 1893; aged 74; died, September 29, of acute dilatation of the heart, arteriosclerosis and nephritis.

J. M. Caldwell, Augusta, Ga.; Medical College of Georgia, Augusta, 1897; at one time demonstrator and instructor of obstetrics at his alma mater; aged 68; died, September 16.

Adolph P. Wohlenberg, Kooskia, Idaho; College of Physicians and Surgeons of Chicago, 1894; formerly a druggist; aged 76; died, September 23, of carcinoma of the prostate.

Alexander Joseph Slaven, Columbus, Ohio; Bellevue Hospital Medical College, New York, 1898; aged 67; died, September 19, of cerebral embolism and arteriosclerosis.

Charles Torbush Haines, Utica, N. Y.; Pulte Medical College, Cincinnati, 1887; on the staff of the Utica Memorial Hospital; aged 75; died, September 30, of heart disease.

Robert C. Wear, Baxter Springs, Kan.; University of Kansas City Medical Department, 1885; member of the Kansas Medical Society; aged 80; died, September 9.

Lawrence Arthur Petty, Charleston, W. Va.; University of Cincinnati College of Medicine, 1913; served during the World War; aged 52; died, September 14.

Benjamin Frank Hutchings, Crawfordsville, Ind.; Medical College of Ohio, Cincinnati, 1872; aged 92; died, September 29, of chronic nephritis and arteriosclerosis.

Bruce Jonas Crisman, Utica, N. Y.; Syracuse University College of Medicine, 1907; aged 56; died, September 29, in St. Luke's Hospital of heart disease.

Rufus V. Gamble, Elyria, Ohio; Western Reserve University Medical Department, Cleveland, 1871; aged 90; died, September 28, of intestinal obstruction.

George Washington Henderson, Westerville, Ohio; Starling Medical College, Columbus, 1892; aged 81; died, September 23, of cerebral hemorrhage.

Johnston Frank, Dallas, Texas; Medical College of Ohio, Cincinnati, 1880; Jefferson Medical College of Philadelphia, 1886; aged 81; died, September 29.

Clarence Woodson Warnock, Huntington, W. Va.; Kentucky School of Medicine, Louisville, 1907; aged 57; died, September 16, in St. Mary's Hospital.

Mary Elizabeth Fetzer Mazza, East Cleveland, Ohio; Western Reserve University School of Medicine, Cleveland, 1928; aged 36; died, September 14.

Samuel Cooke Ingraham, Philadelphia; Jefferson Medical College of Philadelphia, 1886; aged 88; died, September 11, of cystitis, prostatitis and uremia.

Francis Boyd Carleton, Boston; Boston University School of Medicine, 1894; aged 73; died, September 7, at his summer home in Sebago Lake, Maine.

John C. Swatzlander, Fontana, Calif.; University Medical College of Kansas City, Mo., 1897; aged 66; died, September 11, of cirrhosis of the liver.

Napoleon B. Winfrey, Kansas City, Mo.; Kansas City Medical College, 1881; aged 86; died, September 10, of chronic myocarditis and nephritis.

C. E. Smith, Enid, Okla.; Louisville (Ky.) Medical College, 1893; aged 72; died, September 10, in a local hospital of prostatitis and urinary calculi.

Walter Kenney Barrett, Milford, Del.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; aged 68; died, September 10.

Ward Greene Clarke, Chicago; Rush Medical College, Chicago, 1882; aged 79; died, October 27, of coronary and cerebral thrombosis.

Sara May Donnell Wolverton, Merchantville, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1904; died, September 27.

John Francis Heffernan ● Albany, N. Y.; Albany Medical College, 1901; on the staff of St. Peter's Hospital; aged 61; died, September 8.

Walter Davis Wilson, Schlater, Miss.; University of Tennessee Medical Department, Nashville, 1893; aged 71; died, September 23.

Henry Franklin Bean, Portsmouth, Ohio; University of Louisville (Ky.) Medical Department, 1876; aged 85; died, September 11.

Charles Garfield Chapin, Brantford, Ont., Canada; University of Toronto Faculty of Medicine, 1906; aged 54; died, September 26.

Joseph Napoleon Bonaparte Rawls, Brooklyn; Eclectic Medical College of the City of New York, 1899; aged 72; died, September 30.

Andrew J. Allen, Subiaco, Ark.; Gate City Medical College, Dallas, Texas, 1907; aged 70; died, September 20, of pulmonary tuberculosis.

William Lyan Wilson, St. Joseph, Mich.; Detroit College of Medicine, 1890; aged 71; died, September 6, of carcinoma of the prostate.

Adam Hume Millar, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1908; aged 58; died, September 28.

Daniel Paul Odom, Lyons, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1901; aged 68; died, September 25.

Samuel McLean Withers, Moultrie, Ga.; North Carolina Medical College, Davidson, 1902; aged 61; died, September 4.

Hugh C. Cunningham, Roganville, Texas; Jefferson Medical College of Philadelphia, 1885; aged 76; died in September.

William A. Reed, New York; Hahnemann Medical College and Hospital, Chicago, 1880; aged 83; died, September 15.

Waldemar Ude, St. Louis; Marion-Sims College of Medicine, St. Louis, 1892; aged 67; died, September 17.

Bureau of Investigation

TUCKER'S SPECIFIC FOR ASTHMA CRIES HELP!

New Legislation Causes Pain and Anguish to Proprietors of an Old, Old Asthma Specific

As long ago as May 20, 1911, the Bureau of Investigation (then known as the Propaganda Department of the American Medical Association) first called attention to the nostrum "Dr. Nathan Tucker's Specific for Asthma, Hay Fever and Nasal Catarrh." In a Notice of Judgment issued Sept. 29, 1911, the government declared the "specific" misbranded on two counts. Thirteen years later THE JOURNAL (Nov. 1, 1924) pointed out editorially that the Commissioner of Internal Revenue had replied to an inquiry from THE JOURNAL that, while "Tucker's Asthma Specific" carried a label admitting the presence of 5 grains of cocaine to the fluidounce, before the remedy reached the public the cocaine became hydrolized and there was either no cocaine or but an infinitesimal quantity. The commissioner also expressed the opinion that the mail-order distribution of this nostrum served "a great humanitarian cause"; therefore it had been decided by the Treasury Department to take no action enjoining its distribution. THE JOURNAL concluded its comments, in part, as follows:

"If it contains cocaine or a derivative of cocaine, and the Treasury Department has admitted that it does, then its sale violates the Harrison Narcotic Law, for that law applies just as much to the derivatives of cocaine as it does to cocaine itself."

The present promoters of the product appear to be Drs. W. B. and G. B. Robinson, and they are apparently concerned over the effect of the new Food, Drug and Cosmetic Act on their product. According to the Mount Gilead (Ohio) *Sentinel* for Sept. 8, 1938, Dr. W. B. Robinson addressed the local Kiwanis Club in part as follows:

"There are now patients using this remedy in every town of 500 or more population in the entire country, and this has resulted solely from one person securing relief and then telling others.

"Legislation has been recently passed at Washington which will force every such patient to come to Mount Gilead for treatment. [It would indeed be a sight worth seeing if citizens from every town of the United States of more than 500 population were to gather together into a Coxey's army and march on to Mount Gilead.—Ed.] Only a small percentage of such cases can afford to come to Mount Gilead, and as a result of this hasty and ill considered legislation thousands of asthma sufferers will be unable to secure relief.

"Unless an amendment is made to the law, thousands of asthma sufferers who now obtain relief from the use of this remedy will be doomed to suffer indefinitely, many of them all the remainder of their lives, because of their inability to come to Mount Gilead from their homes hundreds of miles away."

This colossal assertion by Dr. Robinson presumes that these sufferers could not obtain more scientific and efficacious treatment by inquiring of their family doctor, or an allergist in their locality, than they obtain at the present time from Mount Gilead.

The Drs. Robinson are so concerned about this matter that a form letter addressed "To Our Patients" is apparently being distributed at the present time. The letter says in part:

"The new law quite properly exempts physicians from its requirements, but into the final draft some influence slipped twenty-one words which provide that diagnosis may be made only after a personal examination."

The letter even goes so far as to admit that, "in treating most of the ills that flesh is heir to, a personal examination is essential [It adds, however] but 48 years of experience, and the statements in our text books have convinced us that this is an unnecessary and an unreasonable requirement when dealing with such characteristic syndromes as Asthma and Hay Fever."

It might be suggested that the Robinsons consult some more recent textbooks for details of skin tests, elimination diets and other means of determining the causative agents in asthmatic conditions. As a result of such tests, causative agents can be frequently eliminated and desensitization to such agents sometimes accomplished. But, of course, this constitutes scientific treatment.

The Drs. Robinson say that they are "delighted to see the continuing procession of patients that come to our office, but experience has doubtless proven that we can relieve your Asthma or Hay Fever without the necessity of a personal examination." Why the "doubtless"?

The concluding paragraph of the form letter is especially interesting. It reads:

"At the next session of Congress we are going to ask for an amendment that will enable us to serve you as we have in the past. If you with our tens and tens of thousands of other patients will bring this to the attention of your Senators and Representative, either by a letter or a personal interview, we are sure our amendment will be accepted. We would appreciate copies of any letters, or report of your personal interview."

A parallel to this form letter was forwarded by Dr. W. B. Robinson "To Our Patients In New York" under date of Feb. 18, 1913. It read as follows:

"The Walker Bill No. 692 has been submitted to the Legislature of New York State. If this Bill becomes a law we cannot send you further fluid.

"If your physician should be fortunate enough to know a prescription that would relieve your asthma he could come to your bedside and give it to you. If, however, it contained cocaine you would render yourself liable to fine and imprisonment if you kept his medicine in your house over ten days; in other words, it would be unlawful for you to have in your possession over ten days any medicine which contained cocaine in any form or in any dosage. This means that if it happened to be eleven days after you received the prescription before you had an attack of asthma, you could not legally use it.

"The purpose of this law is to prevent the indiscriminate sale of cocaine to the drug fiends or in any way that might make drug users. In so far as it accomplishes this it is good. The workings of it, however, we are sure would be a very great hardship to you.

"We trust you will take this up with your Senators and Representatives, or with any prominent people you know in your State; give them your opinion of our Treatment; state to them frankly whether it has relieved you and if it has in any way produced a drug habit.

"If you know any of the Senators or Representatives personally, I would be pleased if you would give me a letter of introduction to them.

"PLEASE ACT IMMEDIATELY."

It is interesting to note the more recent attempt on the part of this nostrum manufacturer to counteract the useful and effective measures which are part of the new Food, Drug and Cosmetic Act. The provisions which make up the new Food, Drug and Cosmetic Act are designed in part to prevent the mulcting of innocent people who believe that they can be treated by "long distance" for conditions which require personal medical attention.

KELPEP, PROSTAX AND GLANMEND

The Frauds of Lord & Company Are Debarred from the Mails

One Mrs. Rose Lord Pressner of Ridgewood, Brooklyn, N. Y., doing business under the trade styles "R. Lord," "Lord & Co." and "Lord's," sold mail-order nostrums for the alleged cure of lost sexual vitality and allied conditions. From the evidence it appears that Mrs. Pressner contacted her victims through advertisements carried in newspapers which are not particular about the type of advertising they accept. She also, it is stated, purchased "sucker lists" from concerns that deal in such merchandise.

In her advertising Mrs. Pressner stated that she had "seen a lot of men worn down Physically and Mentally." She suggested that those who lacked the "power of erection" should take her "Kelpep," which, she claimed, was "number one in building up" and "one single teaspoonful [of which] contains more natural iodine than 427 pounds of spinach" and was "proportionately 700 times richer than oysters." She also recommended her "Glanmend," which she called "the newer tonic tablet treatment" that would "put brand new pep into your tired body almost like magic."

Mrs. Pressner was also solicitous of those who had symptoms of prostate "trouble." She declared that "a man is as old as his prostate." For these she had some rectal suppositories called "Prostax." In addition, as a sideline she added to her armamentarium for those males who lacked vim, vigor and vitality a device that she called "Giant Developer." This was actually a mechanical masturbator of a type that the Post Office has time and again debarred from the mails.

When Lord & Co., et al., were called on last April to show cause why a fraud order should not be issued against them, no person appeared at the hearing but a firm of attorneys forwarded a written answer and certain exhibits. The postal officials

declared that there were no physicians, chemists or pharmacists connected with the business but that Mrs. Pressner was the sole owner and the only person involved in the operation of the business.

Government chemists reported that Kelpep tablets consisted essentially of seaweed with a fraction over one one-hundredth of a grain of iodine to each tablet. The Glanmend "tonic" was found to contain some animal tissue with strychnine and saw palmetto. The strychnine was the only ingredient with a known pharmacologic effect, and the claim that Glanmend would restore sexual vitality was declared fraudulent. The suppositories which were supposed to cure "prostate trouble" were found to have a base of cocoa butter in which were incorporated about 3 per cent ichthammol and small amounts of atropine, hydrastine and oil of juniper. The claim that this would reduce the size of a hypertrophied prostate or eliminate all symptoms of prostate trouble was declared false.

Mrs. Pressner's scheme was declared to be one for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises. The mails were closed to R. Lord, Lord & Co. and Lord's on July 1, 1938.

Correspondence

RACIAL DIFFERENCES IN HYPERTENSIVE DISEASE

To the Editor:—In THE JOURNAL October 29, page 1684, a reply to a query asking about the racial incidence of hypertension stated that there is no well defined racial difference in the incidence of hypertensive disease. This statement is not at all in agreement with the literature, especially that which has to do with hypertension in colored people.

The proneness of Negroes to hypertension and its resultant or concomitant cardiac and renal changes has been noted and studied by several investigators. Adams (*Am. J. M. Sc.* **196**:342 [Sept.] 1932) made several blood pressure readings on each of 5,074 male employees and one reading on each of 9,000 applicants for employment. About one third of these were colored and the remainder white. The average white systolic pressure was 121 mm. and the diastolic 81 mm.; for the colored, systolic 128 mm., diastolic 85 mm. In each age group the Negro systolic pressures were from 4 to 13 mm. higher than those of the white men, and the diastolic pressures were from 2 to 6 mm. higher. Beyond 40 years of age the pressures of the Negroes advanced more rapidly than of the white men. The maximum differences of the average systolic pressures in the age groups occurred at ages 46-50 years and at 56-60 years, when the colored systolic pressures were respectively 11 mm. and 13 mm. higher. The maximum difference in diastolic pressure was in the 41-45 year and 56-60 year groups, which in both instances amounted to 6 mm. over the white. The average of the maximum systolic pressures of all 5 year age groups from 18 to 65 was 205 mm. for the white men and 222 mm. for the Negroes. The average of the minimum systolic pressures was 79 mm. for both races. Damage to the aortic valve in hypertension, as evidenced by an increased pulse pressure, occurs earlier and more frequently in Negroes. Jaffé (*Zentralbl. f. allg. Path. u. path. Anat.* **33**:209, 1922) found, in his necropsy experience at the Cook County Hospital in Chicago, that hypertension and malignant nephrosclerosis were much more prevalent in Negroes and that also the average age at death was lower. Moritz and Oldt (*Am. J. Path.* **13**:679 [Sept.] 1937) made a detailed study of arteriolar sclerosis in a necropsy population of 1,177 individuals. Negroes made up 20 per cent of this population but furnished 30 per cent of the cases of chronic hypertension, indicating again that the disease has a higher incidence among them than among the white men. Analysis of the ages in the hypertensive cases showed that the mean age of the Negroes was eight years lower than that of the white men. These patients with hypertension died of uremia, cardiac failure or cerebral hemorrhage, but about the same percentage of Negroes and white men died of each of these causes. Histologic studies of each type, distribution and severity of arteriolar changes in white and colored nonhypertensive and hypertensive men showed no racial differences.

Schulze and Schwab (*Am. Heart J.* **11**:66 [Jan.] 1936) applied the various theories that have been applied to explain hypertension to account for the difference between white persons and Negroes. They disclaim the role of inheritance, since hypertension is absent in native Africans and there is not enough intermixture with white persons to account for the departure from this African characteristic. Moreover, they say, the mendelian law of inheritance is not in accord with the excess of hypertension in Negroes over white persons, which amounts to 2.5 times. The effect of the change from African to American climate is considered but, although Europeans and Americans show a lowering of blood pressure in the tropics, there is no evidence that the contrary circumstances produce opposite results. Although syphilis is present in Negroes, its role in hypertension is questionable. (The relation of syphilis to hypertension is discussed by Horine and Weiss: *Am. Heart J.* **6**:121 [Oct.] 1930.) Likewise diet and obesity are unsuitable as explanations of hypertension. Schulze and Schwab resort to the theory of nervous factors to account for the high rate of hypertension in Negroes. They believe that the true explanation is the stress and strain incident to adjustment to a new civilization.

Statistics show that arteriosclerosis causes relatively more heart disease and hypertension causes relatively less heart disease in white persons than in Negroes. Stone and Vanzant (THE JOURNAL, Oct. 29, 1927, p. 1473) found that 50.5 per cent of the heart disease in Negroes was caused by hypertension as compared to 45.3 per cent in white persons. Arteriosclerosis produced 19.8 per cent of the cases in white persons and 6.3 per cent in Negroes. In the same clinic a few years later Schwab and Schulze found that 42.4 per cent of the cases in white persons and 63.2 per cent of the cases in Negroes were due to hypertension and 35.9 per cent of the cases in white persons and 13.7 per cent of the cases in Negroes were produced by arteriosclerosis. Arteriosclerosis is a disease primarily of advanced age, and the lower rate of this condition in Negroes might mean a lower proportion of the upper age groups in this race.

Hedley (*Pub. Health Rep.* **50**:1127 [Aug. 23] 1935) points out that Negroes dying in the arteriosclerotic-hypertensive group of heart disease do so at an earlier age than white persons. In his series the average age of Negroes at death was 54.6 years and the average age of white persons was 66.6 years. The peak of deaths of Negroes was at 40-49 years and of white persons it was 60-69 years. In the white persons 40.4 per cent of these deaths occurred at the age of 70 years or more but only 16.7 per cent occurred at this time among the Negroes. Death occurred before 40 years in 0.6 per cent of the white persons and in 12.9 per cent of the Negroes.

Jaffé was of the opinion that the large amount of hypertension in Chicago Negroes was due to their recent immigration from the South.

Polak (*Am. J. Obst. & Gynec.* **4**:227 [Sept.] 1922) says that fibroids, which are very prevalent in Negro women, have no effect on blood pressure, although a relation between these two conditions has been suggested.

Schwab (*Proc. Soc. Exper. Biol. & Med.* **32**:583 [Jan.] 1935) determined the results of the vasomotor test of Hines and Brown (*Ann. Int. Med.* **7**:209 [Aug.] 1933) on 172 white persons and 153 Negroes between the ages of 15 and 35 years. In this test the hand and wrist were put in cold water (from 4 to 5 C. or 39 to 41 F.) and while in the bath blood pressure readings

were taken thirty, ninety and 150 seconds after immersion. He found that the elevation of blood pressure is more marked in Negroes and concluded that there is a quantitative racial difference in reaction to a standard vasomotor stimulus, indicating a more sensitive vasomotor mechanism in the Negro. This evidence is used in support of the neurogenic theory of hypertension.

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Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

AIR CONDITIONING FOR PNEUMONIA

To the Editor:—What is the latest method of treating both lobar and bronchial pneumonia in an air conditioned room in a hospital? What are the advantages? What are the contraindications?

ALBERT C. LUNDGREN, M.D., Minneapolis.

ANSWER.—Whenever a patient is placed in an oxygen tent, the atmosphere surrounding him is conditioned. When tents are well designed and operated, the atmospheric conditions assist cooling and maintain a desired partial pressure of oxygen and of carbon dioxide.

The essential factors in proper atmosphere conditioning have been analyzed and desirable conditions formulated (Bullowa, J. G. M.: Management of the Pneumonias, New York, Oxford University Press, 1937). The factors controlled are temperature, relative humidity, rate of air movement, oxygen concentration, carbon dioxide concentration and removal of noxious substances, either chemical or particulate, which cause odors.

The necessary loss of oxygen and the introduction of surrounding unconditioned atmosphere when services are rendered to the patient are inherent disadvantages in even well designed and operated individual oxygen enclosures or tents. Some patients have a feeling of confinement and isolation. Either the nursing and examinations are neglected in order to retain the high and uniform oxygen concentration or desirable and even essential atmospheric conditions are sacrificed.

In some climates and under some atmospheric conditions and, in the case of less severely stricken patients, uniform high oxygen concentration may be sacrificed in order that better nursing care may be provided and physical examinations performed. Nevertheless, in some late and prostrated patients disaster may follow when, for even brief periods, oxygen concentration is diminished to provide nursing care and careful physical scrutiny.

To overcome these disadvantages, oxygen rooms have been provided in some well equipped hospitals. In them patient and nurse are simultaneously enclosed. Both nursing care and the physician's observations may be provided without loss of optimal atmospheric conditions.

Conditions desirable for febrile anoxic patients may not be agreeable to those entering a well conditioned room from warm or humid surroundings. This may lead to unwise criticism. Recording instruments are accordingly desirable to proper operation of atmosphere control rooms.

Excellent, satisfactory air conditioned rooms are in use at the Rockefeller Institute, the Presbyterian and the Harlem hospitals in New York. Those responsible for the care of patients with lobar and bronchopneumonia in these hospitals believe that they are of great value and do not wish to give them up. In various centers improperly designed chambers have been built without suitable locks, adequate provision for air conditioning or economical maintenance of the oxygen concentration. Naturally, these have proved unsatisfactory and have been abandoned. The principle of air conditioning in the treatment of pneumonias is sound and in practice desirable and may be economical.

The cost of maintaining a well designed, maintained and operated oxygen chamber is not considerably greater than the cost of maintaining an oxygen tent. The first cost of installation is offset in the case of patients desperately ill by the much more satisfactory results.

ESOPHAGOBRONCHIAL FISTULA

To the Editor:—A man aged 32 has had an esophageal-bronchial fistula for several years following a traction diverticulum. There is no evidence of tuberculosis. He has no fever. The blood sedimentation (Westergren) is 30, the leukocytes number 10,100, and the hemoglobin (Sahli) is 100 per cent. He has had several attacks of bronchial pneumonia and complains of violent coughing. X-ray examination shows esophageal-bronchial fistula of a large size and signs of gastritis and cardiospasm. He has been nourished through a duodenal sound with relief. He weighs 79 Kg. What treatment can be followed? Is there any chance of operating without opening the thorax?

L. ZWILLINGER, M.D., Prostejov, Czechoslovakia.

ANSWER.—Nonmalignant esophagobronchial fistulas are rarely observed. Ribbert has suggested a developmental origin, but it is generally agreed that they are usually secondary to traction diverticula caused by the healing of tuberculous lymph glands. Foreign bodies may occasionally be the cause. Death from pulmonary suppuration is almost certain to ensue unless the fistula is closed. It is surprising that the defect can be tolerated over a period of years, but a chronic course is not uncommon.

The condition is so rare that no one has had extensive experience in the treatment. In one case Clerf succeeded in closing the fistula by cauterizing its surfaces with silver nitrate through the esophagoscope. For several weeks subsequent to the procedure, feeding was done through a catheter passed into the stomach. In the case under consideration there are two factors which make it peculiar. These are the cardiospasm and what seems to be a large pulmonary cavity. The obstruction at the lower end of the esophagus and the dilatation of the esophagus must be important in favoring the patency of the fistula and the passage of food through it. Probably the first step in treatment should be to relieve the cardial obstruction. The second should be an attempt to close the fistula by cauterization with silver nitrate. If these procedures are successful the pulmonary suppuration has still to be dealt with. Once the fistula is closed, this may improve sufficiently not to require treatment. Drainage of an abscess or lobectomy for bronchiectasis may be necessary.

The reproduction of the roentgenogram leaves uncertainty as to whether what seems to be a cavity in the lung is truly such a cavity or is barium in the fundus of the stomach which has been displaced upward by an elevated diaphragm.

If the cauterization fails to close the fistula, surgical closure must be attempted. The almost certain presence of extensive pleural adhesions makes the question whether the procedure could be performed extrapleurally or intrapleurally unimportant. Two surgical approaches can be conceived of: direct extrapleural exposure of the diverticulum without mobilization of the lung and mobilization of the lower lobe with coincidental exposure of the tract and lobectomy. In the first procedure two ribs directly posterior to the lesion should be resected through a paravertebral incision and the posterior mediastinum reached by dissecting the parietal pleura from the ribs and vertebral bodies. In the second procedure a long posterior segment of the eighth rib should be resected, the pleural cavity opened widely, the lung freed well to the hilus, the diverticulum located and closed, and a lobectomy performed. In either operation one would anticipate considerable difficulty in locating the diverticulum. A catheter inserted into the fistula through the esophagoscope shortly before the operation should help in localization.

COLLES' FRACTURE AND TYPHOID

To the Editor:—A boy 14 years old was admitted to the hospital with Colles' fracture, which was sustained two weeks before. No treatment was administered for the fracture. The day after coming to the hospital he had a temperature of 101.4 F. Several days later a diagnosis of typhoid was made. What is your opinion as to the proper procedure? Should the fracture be reduced immediately or would it be advisable to wait until the typhoid subsides? What are the complications that may develop in such a case if the fracture is reduced?

MORTON J. EARLEY, M.D., Spangler, Pa.

ANSWER.—Healing of a Colles fracture in a 14 year old boy is so rapid that at the end of two weeks it is unlikely that much could be done in the way of a reduction without an open operation. If the deformity is not bad, readjustment will take place in a child of this age, giving a surprisingly good result without reduction. While typhoid patients stand a general anesthetic reasonably well, the general condition of the patient must be taken into consideration before undertaking even a closed reduction. Typhoid is a general blood infection and is occasionally followed by osteomyelitis. An open operation would be likely to be followed by infection and therefore should not be considered at the present time. The probabilities are that it would be much safer to leave the fracture entirely alone.

NO DRUG TO INCREASE LYMPHOCYTES

To the Editor:—What drugs, if any, stimulate the lymphatic system so as to increase the number of lymphocytes in the blood stream? I have been unable to find any literature on the subject. Is there any drug that will stimulate the lymphocytes, as pentnucleotide does the polymorphonuclear cells?

I. L. CUTLER, M.D., Rutland, Mass.

ANSWER.—As far as is known there are no drugs that specifically stimulate the lymphatic system or the production of lymphocytes. Certain diseases, such as pertussis and infectious mononucleosis, are accompanied by a lymphocytosis, but the cause for this is not known.

RELAPSING FEVER OR TULAREMIA

To the Editor:—A man aged 80 was visiting in the Teton Mountains in Wyoming in the early part of July. A few hours after carrying an armful of wood into the house he noticed on each arm what he thought were ticks. He went to the doctor in the community, who diagnosed his condition as "tick fever." The symptoms were fever, nausea, vomiting, numbness in both arms, elbows and wrists, numbness of the right leg and pain in the back of the neck and in the back. The temperature rose to 105 F. He came home and since that time soreness in the muscles and loss of appetite have persisted. There is elevation of temperature daily to 101 F. My diagnosis is relapsing fever. Could you supply me with the latest treatment of this condition?

M.D., Illinois.

ANSWER.—The symptoms presented by this patient are insufficient for a diagnosis of relapsing fever. In this disease there is an incubation period of from six to nine days between the infected tick bite and the onset of symptoms. The febrile stage lasts three days, followed by an afebrile period of four or five days.

Not all tick bites cause relapsing fever. Numerous persons in the region of Gold Park, Nev., have been bitten by ticks with no untoward consequences. Because of the daily elevation of temperature, tularemia should also be considered.

Diagnosis of relapsing fever rests on finding the spirochetes in a blood smear taken during the febrile stage. Smears should be stained with 20 per cent Giemsa stain for thirty minutes.

For treatment, neoarsphenamine is specific when given in sufficient doses during the period of rising temperature. The same dose as in antisyphilitic therapy is indicated. If inadequate amounts of the drug are used, relapses are more prone to recur.

HUNTINGTON'S CHOREA

To the Editor:—What is the latest treatment for Huntington's chorea? Please list the literature supplementing this information.

MORTON M. STERN, Medical Student, Newark, N. J.

ANSWER.—A search of the literature published in the last five years does not reveal any articles dealing with the treatment of Huntington's chorea nor are there any suggestions as to treatment to be found in the discussion of this condition in the articles found in the late systems of medicine. This question was further taken up with several prominent neurologists and no knowledge of any new treatment was reported.

PULMONARY TUBERCULOSIS IN LABORATORY WORKER

To the Editor:—A man aged 30 is now under treatment for pulmonary tuberculosis. Laboratory reports are positive; physical and x-ray examinations indicate a moderately advanced process with two small cavities in the apex of the right lung. The remainder of the lung appears clear. An exhaustive search of the family history and any possible outside contacts reveals nothing which would indicate a possible source of infection. The patient has worked for the last six years in a diagnostic laboratory doing a moderate number of positive sputum examinations. X-ray examinations of the chest four years ago revealed no evidence of pulmonary tuberculosis. Does pulmonary tuberculosis occur in laboratory technicians as a direct result of their work in a diagnostic laboratory making a moderate number of positive sputum examinations? If so, what is the percentage? What is the likelihood of a man aged 30, in apparent good physical health and having a negative chest roentgenogram, developing pulmonary tuberculosis as the result of his six years' work in a diagnostic laboratory? Could this case be termed an occupational disease under the workmen's compensation act?

EDWARD D. DAKE, M.D., Rome, N. Y.

ANSWER.—Since the patient is 30 years old and the x-ray examination of the chest four years ago revealed no evidence of pulmonary tuberculosis, one should also know whether he reacted to tuberculin at that time. A laboratory worker who makes examinations of sputum containing tubercle bacilli may easily contract an infection provided extreme care is not exercised. In the occasional case there is good evidence of the disease having been contracted in the laboratory; that is, nonreactors have become reactors while at work with no other known contact with tubercle bacilli and have later developed the disease clinically. Even then it is difficult to be certain that the infection was not contracted outside the laboratory. As there are few places where large numbers of laboratory workers are employed, it is difficult to obtain sufficiently large figures to determine accurately what percentage fall ill from tuberculosis. In this case, if no tuberculin test was administered four years ago it would be impossible now to determine when the infection first developed; it may have been many years before the patient was employed in the diagnostic laboratory and the present manifestations could easily be the result of endogenous reinfection.

X-ray examinations of tuberculin reactors are of but little help in detecting the primary tuberculosis complex, since rarely does the roentgenogram reveal such complexes in more than 10 or 15 per cent of the reactors examined. Therefore, unless more evidence is available than negative x-ray observations four years ago, it would be a difficult matter to prove that this man's tuberculosis was contracted in the laboratory so as to be termed an occupational disease under the workmen's compensation act, unless the act in the state in which he resides specifically provides for the development of clinical disease while at work and does not take into consideration the possible earlier origin.

GASTROINTESTINAL UPSETS AND CHLORINE IN DRINKING WATER

To the Editor:—Is it true that for many persons the drinking of chlorinated water leads to stomach and intestinal complaints? Is it true that in many localities people do not fully appreciate that this is the cause of repeated attacks of mild cramps, colic, belching and a host of indefinite gastrointestinal symptoms?

M.D., Minnesota.

ANSWER.—The accepted concentration of chlorine in the purification of water is one part in a million. Chlorine gas reacts with organic material and with water to form unstable hypochlorous acid. It is difficult to understand how such a low concentration of chlorine or chlorine compounds could cause digestive disturbances.

Whipple (Microscopy of Drinking Water, ed. 4, New York, John Wiley & Sons, 1927) states that:

> The chlorination of waters which contain certain organic compounds in solution will cause tastes and odors of different characteristics and degrees of intensity depending upon the nature of the organic matter and its concentration. By-products, tastes and odors should be subdivided into:
>
> A. Those caused by combination of chlorine and algae oils or other vegetable or animal matters.
>
> B. Those resulting from chlorine and specific chemicals such as phenols and cresols.
>
> An overdose of chlorine will mask the chlorphenol taste, but upon heating or otherwise driving off the "free" chlorine, the by-product taste still remains. The product is apparently of low volatility and stable, since boiling away 50 per cent of the sample fails to rid the water of the disagreeable taste.

It is perhaps possible that gastrointestinal upsets, such as flatulence, "sour stomach," constipation or diarrhea, might be due to chemical alterations, but it is much more likely that the chlorination has nothing to do with the disturbances. Many of these are of bacterial origin but are transmitted by way of infected food or by food handlers rather than by water. Another possibility is that inadequate chlorination may permit infections to be transmitted by way of the drinking water. The taste of chlorine leads to the false incrimination of the chlorine as the cause of the disturbance. Boiling the water drives off the "free" chlorine and also kills the bacteria.

IRON INTRAVENOUSLY FOR ANEMIA

To the Editor:—I have been interested in the use of iron preparations administered intravenously in the treatment of hypochromic anemias. Could you give me some information as to their use and their reactions and whether they have or have not been considered by the Council on Pharmacy and Chemistry?

MURRAY W. SHULMAN, M.D., Newark, N. J.

ANSWER.—The intravenous or intramuscular administration of iron in hypochromic anemia is to be condemned in all but extraordinary circumstances. If given in adequate amounts to cure the anemia, it is painful, toxic, dangerous and expensive. Heath and Patek (*Medicine* 16:267 [Sept.] 1937) state that they have never seen a case that responded to parenteral iron which failed to respond equally well to adequate dosage by mouth. (Failure to obtain results with iron by mouth is usually due to inadequate dosage.) Only in cases in which severe diarrhea or some other serious contraindication to oral therapy exists should parenteral treatment be considered. While the Council has accepted one iron preparation for injection (green iron and ammonium citrate, U. S. P.), it is stated in connection with the Actions and Uses as given in New and Nonofficial Remedies that "the Council is not convinced that the intra-

muscular or hypodermic administration of iron yields effects which differ from those obtained by the oral administration; however, the unsettled state of iron therapy and the rather large clinical use of iron by intramuscular or subcutaneous injection appears to justify the provisional acceptance of this preparation."

CHILLS AND FEVER AFTER STRENUOUS PHYSICAL TRAINING

To the Editor:—A man aged 24, weighing 150 pounds (68 Kg.) and 5 feet 10 inches (178 cm.) in height, had been training extensively for two months prior to a track meet, running between 2 and 3 miles plus calisthenics daily, working at the same time from 5 p. m. to 1 a. m. The days before the meet he had fever, chills and a clammy cold sweat over his body lasting for several minutes. July 3, the next day, physical examination was negative, but the development of an afternoon temperature from 101 to 103 F. daily kept him in bed. The hemoglobin was 90 per cent, red cells 5,400,000, white cells 8,000, polymorphonuclear leukocytes 74 per cent, lymphocytes 24 per cent, monocytes 2 per cent. Tests for malaria, syphilis, undulant fever and typhoid were negative. The urine was normal. No focus of infection was found. Pleurisy developed about two weeks after the onset of the first symptoms and a pleural tap was negative and recovery complete. At odd intervals chills and fever would return in one attack and he would be apparently well between them. Could this have been a syndrome precipitated by intensive training or is it possible for a focus of infection to remain "hidden" for so long a period with no other outward signs?

W. A. BALOGH, M.D., Dunellen, N. J.

ANSWER.—The data are, of course, insufficient to permit one to arrive at a diagnosis, but in answering the specific questions raised one would suggest that the illness was probably precipitated by the intensive training and incident exhaustion with a presumed "lowered resistance." On the other hand, certain experiments in animals have shown that extreme fatigue paradoxically seems to increase the resistance to deliberate infection. It is indeed possible for a focus of infection (not necessarily in the sites usually associated with the term) to exist. The history of fever and pleurisy suggests that such a focus may be tuberculous and studies with the roentgenograms, skin test with purified protein derivative, sedimentation rate of the red cells and repeated careful examinations should be made. The weight should be registered regularly. Other evidence of infection must also be sought, particularly in the urethra and prostate.

POSSIBLE ALLERGY TO CATGUT

To the Editor:—Several years ago a patient was operated on for streptococcic salpingitis, cystic ovaries and chronic appendicitis. A suspension of the uterus was also done. The sutures used were chromicized sheepgut, no silk or linen sutures being used, and clips were used to close the skin. Before this time she had no allergy of any sort, but since then, beginning about four months after the operation, she has had chronic hives, especially on the lower half of the body. She attributed these at first to potatoes and found some relief by abstinence from them. Lately the condition has become more severe, especially if clothing made of wool or partly of wool is worn and if lamb or mutton is eaten. Could she have developed an allergic reaction to the sutures left in the body? How could an extract or testing solution be made for a skin test? Since the operation she has become more obese; she weighed 185 pounds (84 Kg.) before and 200 pounds (91 Kg.) after it. Diet and small doses of thyroid brought this weight down to 175 pounds (79 Kg.) in several months.

M.D., Pennsylvania.

ANSWER.—The question of sensitivity to catgut is still in dispute. A number of clinical studies of probable catgut allergy have been reported (Hinton, J. W.: *Arch. Surg.* **32**:197 [Aug.] 1936. Tripp, H. D.: *J. Indiana M. A.* **29**:383 [Aug.] 1935. Kraissl, C. J.: *Surg., Gynec. & Obst.* **63**:561 [Nov.] 1936). Animal experiments, however, have generally failed to confirm the claim that catgut is antigenic (Marconi, L.: *Rassegna internaz. di clin. e terap.* **14**:3, 1933. Friagoni, P.: *Arch. ital. de chir.* **43**:334, 1936). The antigenic relationship between catgut and sheep serum could not be demonstrated by Marchesani in animal experiments (*Ber. ve. d. Versamml. d. Deutsche Eph. Gesellsch.* **40**:233, 1932).

In the case mentioned the following considerations are against the urticaria being due to catgut: 1. Sensitization to chromicized catgut because of its relative resistance to digestion is even less likely than to ordinary catgut. 2. The intermission of four months before the development of urticaria is unlikely as an incubation period because of the length of time. 3. The relationship of wool, lamb or mutton to catgut (sheep intestine which has, however, been greatly altered in its preparation as chromicized catgut) is not established. Wool sensitive patients are not usually sensitive to lamb, and vice versa.

The other more common causes of urticaria (drug sensitization, food sensitization, endocrine disturbance, foci of infection) should be considered first in this patient. However, if it is desired to prepare an extract of chromicised gut, it should be ground thoroughly in a mortar with sand, extracted with physiologic solution of sodium chloride for several days and sterilized by filtration through a bacterium retaining filter. The material may then be tried without dilution and in various dilutions (1:10, 1:100, 1:1,000) by the intradermal method in the patient. A number of "normals" should be tested likewise to ascertain that the extract in the concentration used is not irritating to the normal skin (false positive reaction).

REINJECTION OF ASCITIC FLUID IN CIRRHOSIS

To the Editor:—Is it an approved procedure to reinject intravenously in moderate sized doses (about 500 cc.) ascitic fluid removed in a case of portal cirrhosis? The fluid would be collected aseptically. Isn't the loss of the protein in the fluid, which in this case amounts to from 5 to 18 liters (quarts) every two weeks, a drain on the patient which might be lessened by reinjection?

M.D., Virginia.

ANSWER.—This procedure has been carried out in the past by several investigators in cases of cirrhotic ascites with conflicting results. Most ascitic fluid of this nature contains less than 1 per cent of protein and the colloid osmotic pressure is usually low. It is true that such a daily loss of protein is a serious drain on the patient's reserves; but many cases have been followed over long periods with frequent determination of the serum protein values at stated intervals and in spite of the large loss of protein in the ascitic accumulations these patients are able to keep the serum protein at a fairly constant though subnormal level. In order to get enough protein from ascitic fluid it would necessitate parenteral administration in extremely large amounts. Cumulative experience in this field seems to have demonstrated the fact that repeated blood transfusion and the administration of 6 per cent acacia will more favorably affect the protein content and colloid osmotic pressure than would the injection of protein by the method suggested.

NITROUS OXIDE ANALGESIA

To the Editor:—Do you recommend an anesthetic machine of the Ohio Analgesor type for minor operations such as opening an abscess? Ethyl chloride is all right for the skin but does not relieve the pain of probing. Would some type of glass container of chloroform as used in obstetrics for self administration give adequate relief from pain with safety?

ALEXANDER WINTER, M.D., New York.

ANSWER.—Many minor surgical procedures, such as opening abscesses, may be efficiently carried out under nitrous oxide analgesia. The Ohio Analgesor is a type of apparatus designed for producing nitrous oxide analgesia (not anesthesia) by means of self administration. This apparatus mixes nitrous oxide with air and should be operated by the patient. Attempts to produce anesthesia with this instrument will result in oxygen want. By self administration, satisfactory analgesia is produced in many cases.

Self administration of chloroform has been deemed unwise by many because of the toxicity of the drug even in small quantities. If the quantity of the drug administered is controlled carefully and adequately, it may be used with relative safety. Self administration, as suggested, does not offer adequate control of the quantity inhaled in the majority of cases.

No anesthesic agent, apparatus or technic can be recommended. However, individuals may be recommended for the administration of anesthetic agents. The safety of any drug or method in medicine is largely dependent on the doctor's knowledge of it.

COITUS DURING ANTISYPHILITIC TREATMENT

To the Editor:—I am treating a man and his wife for syphilis. Both patients have had two and a fraction courses of neoarsphenamine (about nineteen injections) and one course of bismuth preparations. They intend to continue treatment. Is it possible or likely that one patient would be cured before the other and that the uncured partner would reinfect the other? No measures for prevention of infection have been used during intercourse. Is it necessary that coitus be curtailed?

M.D., Illinois.

ANSWER.—When both husband and wife are infected with syphilis, no curtailment of intercourse is necessary except so far as contraceptive measures may be desirable for the prevention of pregnancy. It is unwise for a woman with early syphilis to undertake pregnancy until at least a year of treatment has been given.

It is improbable that one patient will be cured before the other and subsequently reinfected by the uncured partner. It has happened that both partners have been cured and that one has subsequently been reinfected from an outside source and has then reinfected the other partner.

INFRA-RED PHOTOGRAPHY AND MALIGNANT CONDITIONS

To the Editor:—In a recent article in Collier's the use of infra-red photography was mentioned as a means of determining the extent of inward growth of tumors appearing in or just beneath the skin. The author stated also that such means give an indication of possible malignant conditions. What is the status of such work? If it is of any value, experimental or otherwise, please outline the technic or cite references.

M.D., North Carolina.

ANSWER.—It is possible by means of infra-red photography to visualize the superficial veins in the skin of subcutaneous tissues. This procedure does not permit a distinction between a benign and a malignant tumor. In its present stage of development it has no value in the diagnosis of neoplastic diseases.

SIMILAC, ORANGE JUICE AND COD LIVER OIL IN INFANT FEEDING

To the Editor:—Since birth a baby has been on a diluted similac formula exclusively. Is this a satisfactory substitute for a whole milk formula over an extended period of time? When should orange juice and cod liver oil be started? The child is now 3 weeks old and has gained nicely.

ALVIN ROSENBERG, M.D., Morristown, N. J.

ANSWER.—Similac in dilutions as recommended at different ages by the manufacturer makes a good formula. It is a satisfactory substitute for a whole milk formula until about 4 or 5 months of age. Orange juice and cod liver oil should be started now, as the infant is nearing 4 weeks of age.

ICE CREAM FOR CHILDREN

To the Editor:—What is considered the proper time to introduce ice cream into the diet of a child? I can find no satisfactory statement on this point in any books to which I have access.

M.D., New York.

ANSWER.—Ice cream is a frozen, sweetened milk product, most often made with the addition of some flavoring extract. If this frozen material is properly prepared and protected against spoiling, it may be given in small quantities to children starting at 18 months or 2 years of age. A caution should be urged that the product be of the purest quality.

TESTES ATROPHY AND TESTICULAR EXTRACTS

To the Editor:—When testicular extracts are administered in the treatment of the benign prostatic hypertrophy or chronic prostatitis is there any danger of producing a secondary atrophy of any of the component cells of the testis in the patient under treatment?

M.D., Idaho.

ANSWER.—There is probably no danger. In immature rats such substances cause severe testicular injury but in mature rats no such effects have been reported. No reports of damage to testes have been reported for man.

ACTION OF MAGNESIUM SULFATE SOLUTIONS SUBCUTANEOUSLY

To the Editor:—Please explain why a 50 per cent solution of magnesium sulfate, although hypertonic, is painless when injected subcutaneously.

M.D., Indiana.

ANSWER.—A solution of magnesium sulfate in the concentration of 0.8 per cent is capable of producing local anesthesia when injected subcutaneously. At this concentration it acts slowly. When the concentration is 50 per cent the action is almost instantaneous, the anesthesia being produced by the action of the drug on the nerve endings and the nerve trunks. Consequently a subcutaneous injection of a 50 per cent solution of magnesium sulfate is painless.

THE SKELETON AND BODY WEIGHT

To the Editor:—To what degree is weight affected by difference in the weight of the skeleton? For instance, what difference in weight would one expect in three men of the same age and same height, one having a frame that would be called heavy, another medium and another light?

W. S. DOUGLAS, M.D., Lewiston, Idaho.

ANSWER.—These queries cannot as yet be answered categorically; there are not enough relevant observations. What may be said definitely is as follows:

The skeletons of persons who have died of prolonged exhaustive illness are as a rule lighter than those of persons of the same age and development who have not been so affected.

In senility the skeleton gradually loses in weight, and in some instances the eventual loss may be considerable. But there is little if any regularity to the process.

During adult life, under normal conditions, the weight of the skeleton is proportionate to the height and robustness of the person. But even here, as in all other features of the human body, there is a range of normal individual variation.

PARALYSIS OF ARM AFTER TIGHT BANDS OR BRACES

To the Editor:—What are the possible effects of shoulder braces or arm bands in causing "peripheral nerve lesions of the arm and forearm"? What procedures are indicated to prevent such injuries?

GREGORY SMITH, M.D., New York.

ANSWER.—Shoulder braces that are too tight may induce sensory and motor paralyses of the extremity of varying degrees. "Crutch paralysis" is of the same character and may last for some weeks. The treatment consists of removal of the cause, such as too tight shoulder braces or bands, and complete recovery may be predicted.

VEHICLE FOR BROMIDES AND BELLADONNA

To the Editor:—Can antipyrine, bromides and tincture of belladonna be combined in a single prescription for whooping cough? I have used the latter two together in a vehicle of syrup of citric acid and cinnamon water, which, however, does not make a pleasant tasting preparation. Could the three be combined in syrup of glycyrrhiza? Is there something better?

M.D., Iowa.

ANSWER.—Antipyrine, bromides and tincture of belladonna may be combined in a single prescription, and the syrup of glycyrrhiza makes a better vehicle for them, as far as disguising the taste is concerned, than does syrup of citric acid and cinnamon water. There is probably no better vehicle for these drugs than syrup of glycyrrhiza.

FAMILIAL SPINAL SPASTIC PARAPLEGIA

To the Editor:—I should like information or references as to any arrestive or preventive medical treatment for familial spinal spastic paraplegia.

M.D., Pennsylvania.

ANSWER.—There is no known treatment that will arrest the course of this disorder. Like other familial diseases, it might ultimately be stamped out if those afflicted should be sterilized.

HAVERHILL FEVER

To the Editor:—Who is equipped to do an agglutination test for Haverhill fever? Kindly give bibliography of this disease.

E. C. ALEXANDER, M.D., Castalia, Ohio.

ANSWER.—Agglutination tests for Haverhill fever can be done at the Division of Infectious Diseases, National Institute of Health, Washington, D. C. Dr. Place at the Boston City Hospital is also equipped to do this test. The following references give a good description of the disease:

Scharles, F. H., and Seastone, C. V.: Haverhill Fever Following Rat Bite, *New England J. Med.* 211:711 (Oct. 18) 1934.

Parker, Frederic, Jr., and Hudson, N. P.: The Etiology of Haverhill Fever (Erythema Arthriticum Epidemicum), *Am. J. Path.* 2:357 (Sept.) 1926.

Place, E. H.; Sutton, L. E., Jr., and Wilmer, Otto: Erythema Arthriticum Epidemicum, Preliminary Report, *Boston M. & S. J.* 194:283 (Feb. 18) 1926.

Hazard, J. B., and Goodkind, Robert: Haverhill Fever (Erythema Arthriticum Epidemicum, THE JOURNAL, Aug. 13, 1932, p. 534.

GARLIC TO LOWER BLOOD PRESSURE

To the Editor:—Is the use of "garlic" of any value in lowering blood pressure in essential hypertension?

M.D., South Carolina.

ANSWER.—No.

TREATMENT OF HEMANGIOMA

To the Editor:—With regard to "Treatment of Hemangioma," page 1683 of THE JOURNAL, Oct. 29, 1938, I should like to suggest a source of solid carbon dioxide available to any practitioner. Not having a cylinder to make carbon dioxide snow, I decided to use commercial dry ice and obtained some from my druggist. Cutting it into appropriate shapes and sizes, I have used it to cure successfully three hemangiomas. The first patient was a baby girl of six months with two pea sized hemangiomas, one in the center of the forehead and the other on the inner aspect of the thigh. The other patient was a girl of six with a smaller spider-like hemangioma on her temple. All were cured without scarring with one fifteen second application each.

FREDERIC SPERR, M.D., Kansas City, Kan.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, Jan. 3-5 and June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ALASKA: Juneau, March 2. Sec., Dr. W. W. Council, Box 561, Juneau.

ARIZONA: *Basic Science.* Tucson, Dec. 20. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

COLORADO: Denver, Jan. 4-6. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Feb. 11. Prerequisite to license examination. Address State Board of Healing Arts, 1895 Yale Station, New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, Dec. 26-27. *Medical.* Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

GEORGIA: Atlanta, June. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 9-12. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

IDAHO: Boise, April 4-7. Dir., Bureau of Occupational License, Mr. D. B. Cruikshank, Rm. 355, State Capitol Bldg., Boise.

ILLINOIS: Chicago, Jan. 24-26. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science.* Des Moines, Jan. 10. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor and Detroit, June 14-16. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, Jan. 3-4. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Jan. 17-19. Sec., Dr. Julian F. DuBois, 350 St. Peter St., St. Paul.

MONTANA: Helena, April 4-5. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science.* Omaha, Jan. 10-11. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: *Reciprocity and oral examination.* Carson City, Feb. 6. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW HAMPSHIRE: Concord, March 9-10. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

NEW JERSEY: Trenton, June 20-21. Address, Dr. William L. Wilbur, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 23-26. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

PENNSYLVANIA: Philadelphia, Jan. 3-7. Sec., Board of Medical Education and Licensure, Dr. James A. Neupher, 400 Education Bldg., Harrisburg.

PUERTO RICO: San Juan, March 7. Sec., Dr. O. Costa Mandry, Department of Health, San Juan.

RHODE ISLAND: Providence, Jan. 5-6. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

VERMONT: Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

WASHINGTON: *Basic Science.* Seattle, Jan. 5-6. *Medical.* Seattle, Jan. 9-11. Dir., Department of Licenses, Mr. Harry C. Huse, Olympia.

WISCONSIN: Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Feb. 6. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, December 3, page 2141.

California June Examination

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports the written examination held at San Francisco, June 28-30, 1938. The examination covered nine subjects and included ninety questions. An average of 75 per cent was required to pass. One hundred and seventy-four candidates were examined, 172 of whom passed and two failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists	(1938) 78.9, 80.3, 80.7, 82.4, 83.7, 83.8, 84.2, 84.3, 85.1, 87, 87.3	(1937)	77.7,
Stanford University School of Medicine	78.1, 78.2, 78.6, 79, 79.1, 79.4, 80.6, 80.7, 80.8, 81, 81.3, 81.2, 81.2, 81.3, 81.3, 82, 82.1, 82.6, 82.6, 82.7, 82.9, 83, 83.3, 83.4 83.4, 83.6, 83.8, 83.8, 84, 84.3, 84.3, 84.3, 84.6, 84.7, 85.1, 85.1, 85.1, 85.2, 85.3, 85.7, 86.1, 86.2, 86.6, 86.6, 86.7, 86.8, 87.2, 87.2, 87.3, 88.3, 88.3, 89.7, 92.1	(1938)	76.6,
University of California Medical School		(1938)	77.2,
	77.6, 77.8, 78.4, 80, 80.3, 80.3, 80.4, 81.1, 81.2, 81.7, 82.1, 82.1, 82.2, 82.3, 82.4, 82.6, 82.7, 82.8, 83.2, 83.4, 83.7, 83.8, 84, 84.4, 84.6, 84.6, 84.7, 84.7, 84.8, 84.8, 84.9, 85.2, 85.3, 85.4, 85.4, 85.7, 86.1, 86.2, 87, 87.4, 87.6, 87.7, 87.8, 88, 88.8, 89.6, 89.7, 90.4		
University of Southern California School of Medicine	82.3, 82.9, 83.1, 83.2, 83.4, 84.1, 84.3, 86.4, 87.3, 88.7	(1938)	79.2,
University of Colorado School of Medicine		(1937)	77.6, 85.2
Northwestern University Medical School		(1924) 83.3, (1938)	89.4
Rush Medical College		(1923)	86.1,
School of Medicine of the Division of Biological Sciences	(1937) 79.9, 80.9, 82.3, 86.7, (1938) 85.9, 86.4	(1937)	83.8
University of Illinois College of Medicine		(1938)	81.8
State University of Iowa College of Medicine	(1937) 80	(1936)	81.2,
University of Louisville School of Medicine		(1936)	79.4
St. Louis University School of Medicine	78.7, 85.8, (1938) 82.4, 86.2	(1937)	76.9,
Creighton University School of Medicine	80.1, 80.8, 81.3, 83.2, (1938) 79.1, 85.4	(1937)	79.7,
University of Nebraska College of Medicine		(1937)	80.6
Columbia University College of Physicians and Surgeons		(1937)	81.7
Long Island College of Medicine		(1937)	81.8
New York Medical College and Flower Hospital		(1937)	87.7
Duke University School of Medicine		(1936)	80.8
University of Oklahoma School of Medicine		(1937)	78.4
University of Oregon Medical School		(1936) 86.8, (1937)	87
University of Pennsylvania School of Medicine		(1936) 85.1,	86.8
Marquette University School of Medicine		(1938) 81.3,	83.6
University of Wisconsin Medical School		(1937)	85.7
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1920) 80.8, (1926)	83.4
Ludwig-Maximilians-Universität Medizinische Fakultät, München		(1912)	78
Universität Heidelberg Medizinische Fakultät		(1912)	96.7

School	FAILED	Year Grad.	Per Cent
University of California Medical School		(1938)	74.7
Schlesische - Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau		(1925)	65.7

Book Notices

Health Insurance with Medical Care: The British Experience. By Douglass W. Orr, M.D., and Joan Walker Orr. Cloth. Price, $2.50. Pp. 271. New York: Macmillan Company, 1938.

An entertaining style and numerous personal illustrations and observations make this book easy reading and illuminative of many sides of the problem of medical care in England. There is also a full treatment of the health activities in England largely based on the "Report on the British Health Services" by P E P (Political and Economic Planning) which presents a much more rounded picture than has been given in previous discussions.

The one contribution which the reader has a right to expect from the first extensive work on this subject by an American physician is an evaluation of the medical service given under health insurance. There is an elaborate attempt to give such an evaluation but it can scarcely be said to be successful.

The key to the entire attitude of the book is found in the statement concerning the sources of information. The authors state that they "arrived well armed with introductions to Big Names in English medicine" but that when they talked with an official of the British Medical Association and showed him their list of names he told them to "use them, but they aren't typical" and added "Let me give you names of men who are in general practice and who have insurance panels; they know the system inside and out." The authors congratulate themselves that "Thus Dr. Hill steered us around a common pitfall." The naiveté of this observation is revealing to any one who has undertaken research in Europe concerning social institutions—he is always met by persons who are anxious to show him around and to guide him to the "proper" sources of information; these are often persons who will present the facts that will most surely support the system. That is clearly what happened to the authors of this book.

One of their first informants said he had never "heard of any one getting favors from the doctors or otherwise taking advantage of the scheme." It must have required careful isolation to keep from finding persons who have heard of such things, because they are complained of in official documents and in medical journals and are topics of conversation almost everywhere. In spite of being so carefully guarded, the investigators seem to have run into some of this information, for they say "Some doctors may be hoodwinked or cajoled into

certifying patients as incapable of work when in reality they should not be certified; some may find it profitable to be known as an 'easy doctor.'" Of "sick visitors" we are told that "protection of funds against malingerers is the sole motive" of their visits. The familiar statement that few visits are made by regional medical officers "to inquire into excessive prescribing" and "in only six cases were fines imposed" fails to tell of the continuous flood of letters that are sent out by these regional medical officers politely and mildly warning physicians against such prescribing, and of course nothing is said of the many complaints in official reports, including those of the Ministry of Health, of the excessive prescribing as the result of the efforts of the physician to satisfy the demands of the patient for what British physicians in their own journals frequently admit are unnecessary medicines.

We are informed that "those who assert . . . that N. H. I. has increased the burden of sickness or dodged its responsibility by shifting it to the voluntary hospitals are misrepresenting the facts" (page 85). Yet we are told only two pages earlier that one investigator "found several two to three hundred bed hospitals with waiting lists of five to six hundred each." It must have been difficult even to ride along the roads of England and not see the repeated appeals for financial aid for hospitals and not to be told continuously that this was largely due to the increased burden created by national health insurance.

Perhaps the sharpest criticism which can be directed against the authors is that they base their main arguments as to the good quality of the medical service on the statements of patients. Certainly no physician in this country would accept the fact that a quack or distributer of nostrums can produce thousands of testimonials to the efficiency of his services or of the panacea sold as proof that these were of value to the patient. Yet that is essentially the sort of evidence which is offered here. Certainly, any physician undertaking an experiment with any method of treatment would be expected to produce vital statistics as one measure of the success of his plan. This measure is almost entirely omitted. The statement that "in Britain national concern over a maternal mortality rate which nevertheless averages considerably lower than that of the United States has provoked vigorous action" is not justified in view of the fact that the maternal mortality rate for England was 41.1 per thousand, for Wales 55.7 and for Scotland 63.7, as an average for the years 1924-1933 (Report on Maternal Mortality in Wales, Ministry of Health, London, 1937) while, in the United States, Rhode Island, Wisconsin, Minnesota and several other states show a rate approximately the same as that of England and nearly all the states at all comparable as to climate and racial conditions show rates lower than Wales or Scotland (Vital Statistics—Special Reports 8:43 [March 1] 1938, Department of Commerce, Bureau of the Census, Washington, D. C.). The impression is conveyed that a 40 per cent decline in the death rate during the last forty years in London is in some way related to sickness insurance. The decline in the United States has been even greater, without sickness insurance.

The authors quote "one of the most authoritative persons we interviewed" as concluding that "a panel of 2,500 is not too many for a doctor who has also some private practice." The statistics presented by the British Medical Association in a recent discussion of the capitation rates of payment for physicians showed that a little over five combined office and house calls per insured person were required annually. A panel of 2,500 would require 125,000 such services a year, or about forty for each working day. Considering that other studies of the British health insurance system have shown that these services are much more numerous in certain seasons than in others, we gain a rather peculiar idea of the standard of good service which the authors must have had in view. If we were to use their own figures, which are as much in error as some of their conclusions, this calculation would show much worse conditions, because they quote one of their medical authorities who thinks that panel patients average about ten visits a year. It is strange that authors who say so much about the thoroughness of their investigation and publish so long a list of persons interviewed and so extensive a bibliography did not check these statements with available official statistics.

The bibliography itself requires some little attention. The list of "pamphlets and reports" consulted omits the "Report by the Government Actuary on an Examination of the Sickness and Disablement Experience of a Group of Approved Societies in the period 1921-27" and also the "Report on Incapacitating Sickness in the Insured Population of Scotland during the year 1st July 1934 to 30th June 1935." Is it possible that this omission is due to the fact that these official reports contradict many of the conclusions of the book as to the character of the service given? The entire bibliography is principally noteworthy for its complete omission of a considerable number of books that have been published in Great Britain criticizing health insurance.

There is frequent reference to the way in which disease is supposed to be prevented by early attendance under sickness insurance. No mention is made of Scottish and British reports which complain that immunization for diphtheria lags behind American standards. The authors could have found much information contradicting their statements as to this feature of British health insurance by an examination of the "First Lecture of a London Postgraduate Course" on "Preventive Treatment and the General Practitioner" contained in the Supplement to the *British Medical Journal* for April 1938 as well as in numerous other publications favorable to health insurance. The difficulty which it is claimed existed in finding any opponents or antagonistic critics might have been overcome by a consultation of the correspondence columns of the *British Medical Journal* and the London *Lancet*.

Finally, the attempt to show that British health insurance conforms to the "ten principles" of the American Medical Association is a heavy strain on both facts and logic.

The Doctrine of Signatures: A Defense of Theory in Medicine. By Scott Buchanan. Cloth. Price, $2.75. Pp. 203. New York: Harcourt, Brace & Company; London: Kegan Paul, Trench, Trubner & Co., Ltd., 1938.

This volume in the International Library of Psychology, Philosophy and Scientific Method under the editorship of Prof. C. K. Ogden of Cambridge University belongs in section C devoted to scientific method. In it a metaphysician prescribes a program for physic. He reverts to the classics, in which philosophy had a leading part, and shows how Plato, Aristotle and Galen established the demonstrative power of form and matter in the biologic and medical sciences, and pleads that its rediscovery and reestablishment in modern signatures would reinvigorate medical thinking and open new paths for released speculative energies now thwarted by the lack of an organized philosophy of medicine.

The doctrine of signatures assumes that the data of science are potential symbols and it calls on the liberal arts and sciences to develop, clarify and realize the potentialities of human observations. The practice of these arts and sciences ends in the discovery and formulation of abstract form through which the data achieve their status as facts and scientific evidence. Forms are not only what the signatures signify, they are also the causes of things and therefore the proximate subject matter of science. The author proceeds to show how Plato, Aristotle and Galen elaborated this theme and he ultimately arrives at teleology in Galen. This he interprets as none other than the principle of causal determinism of modern science explained and stated in its fulness in the light of its metaphysical implications. He urges physicians to familiarize themselves with Galen's philosophy of medicine and his concept of physiology, which may be summed up in the title of one of his chapters, The Human Body as Artist.

He has a vision of a fusion of interests of medical men and philosophers in cooperation in establishing a new and more rational organization of scientific thought that has a basis broad enough to include in its scope not only the therapeutic approach to disease but the ramifications of this rationally organized science into legal, social and religious fields. The central position of the medical sciences with reference to man offers inviting prospects of leadership to the organizers of

such a system of thought. "Physic should recover its lost humanism and its intelligibility *quoad nos* as well as *secundum se*."

The proposed program includes the following suggestions, the accomplishment of which in a number of instances is at least in the early stages of formulation or even accomplishment: A critical evaluation of the sciences on which the medical arts depend with special attention to their past uses and their possible future relevance to an integrated science of physic. The abstraction and reformulation of the first principles in these sciences, showing their subordination or interdependence inside a single science. A digest of current working hypotheses, instruments and technics in medical research and practice. A study of measurement in science, numerical and non-numerical. The construction of a rational science and an empirical science of physic based on the preceding studies. A study of medical casuistry, the applied sciences of medicine, diagnosis, prognosis, therapy. A study of social medicine, epidemics, preventive medicine, creative medicine, and the proposed agencies for the medical control of society and the social control of medicine. A study of the possibilities of a permanent board for the continuous criticism and codification of medical knowledge. The last proposal has in it the element of undesirable bureaucracy. Growing sciences do not lend themselves to lasting codification. A certain amount of helpful criticism can be secured through annual topical summaries by experts. An excellent feature in the sciences is found in annual summer conferences in which specialists meet for discussion of live topics, and conflicting views are exposed to criticism. A splendid example is the recently established Mikkelson Foundation of Bergen, Norway, endowed by the statesman-diplomat who composed the political differences between Norway and Sweden. Its policy is to foster annual international gatherings of specialists in the various fields of the sciences and other forms of human intellectual activity for several weeks of common residence, round table discussions and mutual criticism, but without any commitments or decisions by the assembled body. In the field of medicine the annual gatherings appear to be dominated by professional and social trends rather than by those of the programs outlined. Useful as such gatherings are, there still may be a place for the quiet contemplation and discussion of the basic scientific and metaphysical aspects of physic which the author of these prolegomena of medicine has thought out.

Voice for Speech. By Frederick Wesley Orr, Professor of English and Director of the Division of Speech at the University of Washington. Cloth. Price, $2. Pp. 283, with 17 illustrations. New York & London: McGraw-Hill Book Company, Inc., 1938.

The author states that his aim is to contribute in a broad sense to the education of the student and at the same time to attack specifically his voice problems in a basic, fundamental way. At the beginning he points out that "if the author has learned anything during the past ten years in regard to vocal training, it has been the necessity of discovering the cause of the vocal difficulty, whether it be in the thinking, the lack of emotional control, objectionable personality traits, or a defective vocal apparatus; and once the cause has been discovered, working specifically for the removal of that cause." His approach is both physiologic and psychologic, and he believes that any corrective program must take into consideration the entire personality of the individual: the physical condition of his vocal apparatus, its responsiveness to stimulation, and the interferences—including abnormal personality traits and bad vocal habits—which prevent a normal functioning. For purposes of study he divides the vocal apparatus into four different systems; the coordinating system, the breathing system, the tone initiating system and the tone modulating system. He devotes a section to each system, discussing its anatomy and physiology, the abnormalities in its functioning, and the methods of discovering such abnormalities as well as methods of establishing the normal. The remaining four sections are devoted to quality, pitch, duration and strength, and modulating tone into speech sounds. The author suggests a series of tests to determine the reliability of the physical apparatus, especially the sense organs, and in each section he gives a diagnostic chart so that a record may be kept of the results of the tests made. A number of exercises and reading selections are also given in each section. The book covers a great deal of ground and is written with admirable simplicity. However, the arrangement of the material, with its many repetitive divisions and subdivisions, is somewhat complicated, although at the same time it has merit in that each section is a complete unit and, if so desired, can be studied entirely apart from the rest of the material. All in all, the book is a sensible one and to those interested in the subject it should prove useful.

Spectrochemical Abstracts 1933-1937: Being a 52 Page Bibliography with Abstracts of Over 200 Papers on Spectrochemical Analysis. By F. Twyman, F.Inst.P., F.R.S. Paper. Price, 4s. Pp. 52. London: Adam Hilger Limited, 1938.

Twyman is a personality in the field of spectroscopy and applied optical measurement. His spectrochemical abstracts compile the literature of spectroscopy during 1933-1937. There are fifteen pages of author references arranged alphabetically. The remaining thirty-four pages are classified into biologic material, earths, electrodes, gases, industrial materials, liquids, metals and alloys, minerals, nonmetals, oxides, precipitates, soils, apparatus, methods, general, and a list of books. Any active worker in spectroscopy has his own filing system. The value of Twyman's references lies in his careful selection of manuscripts. There are, of course, certain omissions of literature data and larger treatises on spectroscopy, but they will be noted by the modern spectroscopist. In general, the little brochure is a handy tool on the table of any scientific worker making use of spectroscopic apparatus.

New Creations in Human Beings. By Louis Berman, M.D. Cloth. Pr.v., $3. Pp. 316. New York: Doubleday, Doran & Company, Inc., 1938.

Those men who read Berman's book on glands and personality will be prepared to find in this volume the same mixture of science and what David Starr Jordan used to call sciosophy, or the shadow of wisdom. Again in this book Berman's thesis is that internal secretions have much to do with determining the character of the individual, so much so in fact that in many cases criminality can be cured by treating the patient with mixtures of desiccated glands.

Although no expert clinician would question the fact that persons suffering from glandular disturbances are inclined to be nervous, psychopathic and unhappy, few real experts in the field of glandular diseases would care to go so far as Berman does. One difficulty with Berman is that he has his own ideas of what constitutes the clinical picture of disturbances of function in glands such as the parathyroid and adrenal, ideas that do not coincide with those of most scientific physicians today. For instance, on page 41 he tells of a child brought to him because of her shyness, impulsiveness, "explosive assaultiveness," nervousness, poor appetite, insomnia, laziness and dulness at school. Because Berman found a low blood calcium he states categorically that all the girl's troubles were due to parathyroid insufficiency. He does not go on to say how beautifully she reformed on dried parathyroids swallowed three times a day.

On page 253 one finds a description of a burglar who was in and out of reformatories and Sing Sing for eighteen years. He had a persistent thymus gland; "the adrenals were rated as quite deficient, and the gonads and sex glands as moderately deficient." Another bad boy running around and getting into mischief had hyperthyroidism, persistent thymus and marked parathyroid deficiency. According to Berman "There is now a fair degree of certainty that the criminal has a combination of glandular disturbances as the background of his antisocial behavior" and that the way to get at the criminal diathesis is to eradicate these glandular disturbances in childhood.

After many sad experiences in practice, the reviewer cannot help wondering whether Berman's case of hyperthyroidism was diagnosed from a basal reading of + 10 per cent, and the hyperparathyroidism from one blood calcium of 9 mg. reported by a careless, poorly trained technician. The reviewer happens to have seen several cases of serious parathyroid disease but he cannot remember having noted in the patients any great disturbance in character and certainly there was no sign of crimi-

nality. Actually, the patients were complaining of such things as a painful caving-in of the spine, polyuria or tetany. Similarly, the many patients seen by the reviewer with an adrenal tumor or Addison's disease did not show any criminal tendencies.

Berman's answer would probably be that the symptoms that he observes are those of early, mild and unrecognized changes in the glands, but the objection to that is that, if certain symptoms are not found when the disease is severe and recognizable, how can any one prove that they are characteristic of the disease in those early stages in which most experts would refuse to accept the diagnosis? We fear this book should be sold over the fiction counter.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Failure to Discover Disunion of Fracture.—The plaintiff, a woman about 55 years old, injured her left hip Dec. 18, 1932. The next day, on the advice of her attending physician, the defendant, she was removed to a hospital, where roentgenograms disclosed an intracapsular fracture of the neck of the left femur. The defendant reduced the fracture and immobilized her left leg in a splint. Roentgenograms taken five days later showed that the fracture had been reduced satisfactorily. On Jan. 12, 1933, roentgenograms disclosed a bony union and that the fragments of bone were still in good alinement. The patient left the hospital Jan. 23, 1933. Two weeks later, about seven weeks after the injury, the defendant removed the splint and advised the plaintiff to get up and walk with the assistance of crutches. When she attempted to do so she exclaimed "My God, my hip isn't together, I can feel it grating," and then fainted. Although she repeatedly informed the defendant that she believed her "leg was not together," he failed to take or advise the taking of another roentgenogram. On June 15, 1933, the plaintiff went to a clinic, where roentgenograms showed disunion of the fragments of bone. An operation was subsequently performed by another physician, an orthopedic surgeon, but the end result was that she had a 50 to 75 per cent disability. She then sued the defendant for malpractice, the trial court directed a verdict in favor of the physician, and the court of appeals, Summit County, Ohio, affirmed the judgment rendered on the directed verdict. The case was then certified to the Supreme Court of Ohio.

In the judgment of the Supreme Court, the evidence showed that the bony union which takes place between fragments of bone following a proper reduction of a fracture of the neck of the femur may be followed by a disunion through absorption within a few weeks. Such disunion can be disclosed only by a roentgenogram. Accepted medical practice requires that a roentgenogram should be taken at the time the absorption can reasonably be expected to have taken place, if at all, to determine whether that absorption has occurred. In the instant case the defendant failed to take or advise the taking of roentgenograms when the plaintiff complained to him that she felt a grating sensation when she attempted to walk and that the fragments of bone were not together, which was at about the time an absorption might be expected to have taken place. The court was of the opinion, therefore, that the evidence was sufficient to warrant submission to the jury of the issue of the defendant's negligence.

But, continued the court, in order to recover damages the plaintiff must prove not only negligence or unskilfulness on the part of the defendant but also that his negligence or unskilfulness was the proximate cause of her injury. The uniting of fragments of a broken bone must be accomplished by the healing processes of nature and essentially there is always the possibility that nature will fail to achieve the desired result even when the attending physician has done properly everything known to surgical science. Similarly, if the physician's treatment has been unskilful or negligent and the broken parts fail to unite, there is also the possibility that the disunion would have resulted even had the physician used due care and skill. Proximate cause in the present case was an ultimate fact to be proved by the plaintiff and, before the trial court could submit the case to the jury, there must have been evidence which would warrant the jury in drawing an inference of probability. There was, the court said, no such evidence in the record. In fact, the evidence showed that there was a lesser probability rather than a greater that bony reunion would have taken place.

The evidence showed, the court said, that the chance of reunion of the fragments of the bone on a remanipulation and resetting was lost because the defendant had let the patient go on walking with crutches for three months without taking a roentgenogram or giving other attention to the fracture. There was no evidence, however, to show that reunion would have taken place even with the best of treatment. The evidence was therefore insufficient, in the opinion of the court, to support an inference that if the chance had not been lost through the fault of the defendant the injury concerning which the plaintiff complained would not have occurred. Loss of chance of recovery, standing alone, is not an injury from which damages will flow.

Accordingly, the Supreme Court affirmed the judgment in favor of the defendant physician.—*Kuhn v. Banker (Ohio), 13 N. E. (2d) 242.*

Workmen's Compensation Acts: Compensability of Death from Strangulation of Preexisting Noninduстrial Hernia.—From the strain and effort of lifting sacks of material in the performance of his duties, a loop of intestine was forced into the sac of an inguinal hernia from which the deceased already suffered. There the intestine became strangulated. In the course of an operation to release the strangulation, a general anesthetic was administered. Pneumonia followed and death ensued. The industrial accident board awarded compensation to the widow and minor daughter of the deceased. The plaintiff in this case, the employer's insurance carrier, sued to set aside that award. The trial court entered judgment in favor of the plaintiff insurance company, and when that judgment was reversed by the court of civil appeals of the second supreme judicial district, Texas, the insurance company appealed to the Supreme Court of Texas.

According to the pleading, said the court, the injury sustained by the deceased was in final analysis the strangulation of a part of his intestine. This strangulation resulted from the strain of lifting the sacks of material. The strangulation and the ensuing consequences fall clearly within the statutory definition of "injury." The preexisting hernia was incidentally involved in the occurrence of such an injury, but it did not itself constitute the injury or result from it. Nothing appears in the statute, said the court, on which to found a reasonable conclusion that the legislature intended to impose the limitations laid down by it on claims based on hernia, on any injury where no hernia is involved except a preexisting hernia which does nothing more than furnish a condition in which the force which causes the injury operates.

The judgment of the court of civil appeals, reversing the trial court's judgment and remanding the cause for trial, was therefore affirmed.—*Aetna Life Ins. Co. v. Liles et al. (Texas), 114 S. W. (2d) 534.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Memphis, Tenn., Jan. 15-19. Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.

American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 28-30. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N.W., Washington, D. C., Secretary.

American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Boston, Jan. 11. Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Sioux City, Iowa, Jan. 19-20. T. R. Gittins, Davidson Bldg., Sioux City, Iowa, Chairman.

Southern Section, American Laryngological, Rhinological and Otological Society, New Orleans, Jan. 14. Dr. Francis E. LeJeune, Maison Blanche, New Orleans, Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, Spokane, Wash., Jan. 29. Dr. Frederic G. Sprout, Medical Arts Bldg., Spokane, Wash., Chairman.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

196: 609-760 (Nov.) 1938

Protein Production and Exchange in Body Including Hemoglobin, Plasma Protein and Cell Protein. G. H. Whipple, Rochester, N. Y.—p. 609.
Leukopenic Leukemia of Myeloblastic Type. F. R. Miller and W. B. Seymour, Cleveland.—p. 621.
Observations on Blood Regeneration in Man: III. Rise in Reticulocytes in Patients with Hematemesis or Melena from Peptic Ulcer. E. Schiødt, Copenhagen, Denmark.—p. 632.
Peritoneal Lavage in Treatment of Renal Insufficiency. J. E. Rhoads, Philadelphia.—p. 642.
Concentration of Individual Phosphatides (Lecithin, Kephalin, Ether-Insoluble Phosphatide) and of Cerebrosides in Plasma and Red Blood Cells in Pernicious Anemia Before and During Liver Treatment. E. Kirk, Copenhagen, Denmark.—p. 648.
Observations Made on Group of Employees with Duodenal Ulcer. Janette Jennison, New York.—p. 654.
Anorexia Nervosa and Pituitary Cachexia. W. J. Bruckner, C. H. Wies and P. H. Lavietes, New Haven, Conn.—p. 663.
Phenolphthalein Studies: Phenolphthalein in Jaundice. F. Steigmann, R. D. Barnard and J. M. Dyniewicz, Chicago.—p. 673.
*Chronic Hypoglycemia: Problem in Carbohydrate Metabolism. S. Dorst, Cincinnati.—p. 688.
Pulmonary Pneumocyst: Report of Enormous Solitary Cyst in a Healthy Adult Female. G. Cheney and L. H. Garland, San Francisco.—p. 699.
Spontaneous Pneumothorax. J. J. Kirshner, Philadelphia.—p. 704.
*Comparison of Etiology, Death Rates and Bacteremic Incidence in More Frequent Primary Pneumonias of Infants, Children and Adults. J. G. M. Bullowa and M. Gleich, New York.—p. 709.
*Benzedrine Sulfate in Persistent Hiccup: Report of Two Cases. M. S. Shaine, New York.—p. 715.
Standards for Maximal Reticulocyte Percentage After Intramuscular Liver Therapy in Pernicious Anemia. R. Isaacs and A. Friedman, Ann Arbor, Mich.—p. 718.

Chronic Hypoglycemia.—During a period of eighteen months Dorst observed sixty-two ambulatory patients who had low dextrose tolerance curves. From this it would seem that the existence of chronic hypoglycemia is far more common than is generally appreciated and that it frequently occurs in asthenic undernourished individuals who present the familiar picture of the "effort syndrome." The constantly low level of blood sugar may be responsible in part at least for the lack of vigor which characterizes these people, since the chief source of energy in mammalian metabolism is derived from the burning of carbohydrate. Patients with chronic hypoglycemia show a dextrose tolerance curve which remains in the fasting zone regardless of the ingestion of food and it is possible that under these conditions there is inadequate fuel to be suddenly expended in the form of energy. This syndrome must be differentiated from spontaneous hyperinsulinism. When treated with small doses of insulin (5 units before breakfast and 10 before lunch and dinner) a number of the patients with chronic hypoglycemia showed marked clinical improvement, an increase in the sense of well-being, gain in weight and increased appetite; concomitant with this improvement the dextrose tolerance curve returned to the usual normal configuration. The precise action of the insulin in effecting this change is not understood. The author suggests the possibility that the demobilization of hepatic glycogen is in some way inhibited and he hopes to establish this thesis by further investigation.

Etiology, Death Rates and Bacteremia in Pneumonia.—In this article Bullowa and Gleich use the following terms to mean: infants as "children less than 2 years of age," children as "those from 2 years to puberty" and adults "all those beyond puberty." Only the ten commonest of the thirty-two Cooper types of pneumonia are considered. The total number of pneumococcic pneumonias was: infants 381, children 371 and adults 3,065. The ten types of pneumococci represented 63 per cent of all pneumococcic pneumonias in infants, 78.8 per cent in children and 74.5 per cent in adults. The mortality for these ten types of pneumonia among adults was 26.9, infants 16.2 and children 4.1 per cent. In the pneumococcic pneumonias the blood was most frequently invaded in adults (23.5 per cent). The rate for infants was 6.7 and for children 4.1 per cent. In the positive blood culture cases, infants showed the highest death rate (83.3 per cent), adults 74.1 and children 25 per cent. The four important classifications of nonpneumococcic pneumonias represented 66.7 per cent of all nonpneumococcic pneumonias in infants, 84.3 in children and 76.6 per cent in adults. In these cases the death rate was 29.8 in adults, 21.2 in infants and 4.6 per cent in children. In the nonpneumococcic pneumonias, the blood was most frequently invaded in adults (16.1 per cent). In infants it was 4 per cent and for children 1.7 per cent. In the positive blood culture cases, infants showed the highest death rate (100 per cent), adults 95 per cent and children 75 per cent.

Amphetamine Sulfate in Persistent Hiccup.—Shaine found amphetamine sulfate to be of value in relieving two cases of persistent hiccup. In both cases it is apparent that amphetamine sulfate, perhaps through its action on smooth muscle, controlled the spastic condition responsible for the hiccup. The dose of amphetamine sulfate was from 10 to 20 mg. once or twice daily.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

22: 669-818 (Nov.) 1938

Provision of Treatment for Genito-Infectious Disease in the Indigent. N. A. Nelson, Boston.—p. 669.
*Sulfanilamide: Study of Its Effect on Bactericidal Power of Whole Blood for Gonococcus. C. S. Keefer and L. A. Rantz, Boston.—p. 679.
Sulfanilamide Therapy in Hospitalized Gonorrhea. J. F. Mahoney, C. J. Van Slyke and J. D. Thayer, Stapleton, N. Y.—p. 691.
Laughlen Test as Compared to the Kahn and Modified Kolmer Serodiagnostic Tests for Syphilis. R. B. Dienst and E. S. Sanderson, Augusta, Ga.—p. 699.
Influence of Sulfanilamide on Gonococci and Gonococcic Infections. R. D. Herrold and E. Palmer, Chicago.—p. 705.
Quantitative Provocative Reactions in Normal and Syphilitic Serums Following Injection of Neoarsphenamine. C. W. Barnett, G. V. Kulchar and R. B. Jones, San Francisco.—p. 712.
Suggestions for Elevating Standard of Gonorrhea Clinics. M. Wishengrad, New York.—p. 717.
Absorption and Elimination of Bismuth Following Its Oral Administration to Rabbits. E. K. Stratton, San Francisco.—p. 728.
Bismuth Studies: VII. Bismuth Distribution in Dogs Following Intramuscular Injection of Single Dose of Various Bismuth Preparations. T. Sollmann and Katharine Henderson, Cleveland.—p. 739.
Extragenital Syphilis as Described in the Early Literature (1497-1624), with Special Reference to Focal Epidemics. E. L. Zimmermann, Baltimore.—p. 757.

Sulfanilamide and Gonocidal Power of Whole Blood.—Keefer and Rantz show that the administration of sulfanilamide by mouth in adequate amounts to patients with gonococcic infection is followed by an increase in the bactericidal power of the blood for the gonococcus. That this is due to the presence of sulfanilamide and not to the development of specific antibodies was shown by giving the drug to noninfected individuals and by adding the drug directly to whole blood of individuals with and without antibodies. The addition of the drug to serum was as effective as adding it to whole blood, showing that cells and phagocytosis were not necessary for the killing of the gonococcus in these experiments. Heating the plasma to destroy normal antibody reactions did not affect the action of sulfanilamide on the gonococcus. When the drug is discontinued, the concentration in the blood declines rapidly so that within from forty-eight to seventy-two hours most of the sulfanilamide has disappeared. The exception to this is the presence of renal insufficiency. Under these conditions the blood may continue to show large amounts of sulfanilamide for many days. When sulfanilamide is added to ascitic broth there is evidence for a bacteriostatic effect except when small numbers of organisms are used in the original inoculum. Under these circumstances the organisms fail to survive. In the treatment of gonococcic infections maximal effects can be obtained by giving 5 Gm. of sulfanilamide daily and by keeping the sulfanilamide concentration of the blood at 5 mg. per hundred cubic centimeters of blood. The presence of sulfanilamide in the blood and the synovial fluid will aid in the destruction of organisms in the joints and it will also aid in preventing the spread of organisms from a local focus, but it will not cause complete sterilization

of a local focus of infection in the genital tract in every case. Before complete recovery can take place the defense mechanism of the body must increase or retain the capacity to destroy organisms in the local focus. The administration of the drug should be continued until immune bodies have developed.

American Journal of Tropical Medicine, Baltimore

18: 437-624 (Sept.) 1938. Partial Index

Yellow Fever Vaccination with Cultured Virus (17D) Without Immune Serum. H. H. Smith, H. A. Penna and A. Paoliello.—p. 437.
Beriberi or Inanition? I. Effect of Starvation, With and Without Vitamin B_1. E. B. Vedder and A. B. Chinn, Washington, D. C.—p. 469.
Id.: II. Administration of Vitamin B_1 to Rats Receiving Unbalanced Diets. E. B. Vedder, Washington, D. C.—p. 477.
Vernal Vivax Activity in Persons Simultaneously Inoculated with Plasmodium Vivax and Plasmodium Falciparum. M. F. Boyd and S. F. Kitchen, Tallahassee, Fla.—p. 505.
Deficient Homologous Immunity Following Simultaneous Inoculation with Two Strains of Plasmodium Vivax. M. F. Boyd, W. H. Kupper and C. B. Matthews, Tallahassee, Fla.—p. 521.
Effect of Small Amounts of Quinine Administered on a Single Day on Subsequent Course of Infections with Plasmodium Vivax and Plasmodium Falciparum. M. F. Boyd and S. F. Kitchen, Tallahassee, Fla.—p. 525.
Final Report on Use of Atabrine in Prophylaxis and Treatment of Malaria. W. N. Bispham, Baltimore.—p. 545.
Lesions of Syphilis in American Indians. G. C. Shattuck, Boston.—p. 577.
*Venereal Fusospirochetosis. E. von Haam, Columbus, Ohio.—p. 595.
Studies on Oxyuriasis: VII. Clinical Improvement Following Treatment with Single Doses of Tetrachlorethylene. W. H. Wright, J. Boricevich and L. S. Gordon, Washington, D. C.—p. 609.

Venereal Fusospirochetosis.—During studies on the etiology of pudendal infections von Haam encountered progressive and destructive ulcerations of the external genitalia which originated usually, but not exclusively, in the mucous membrane and exuded a copious, purulent, hemorrhagic discharge of penetrating fetid odor. Smears from the exudate showed much necrotic cellular material with numerous pus cells and an abundant amount of fusiform bacilli, spirochetes and vibrios, the characteristic flora of Vincent's infection of the mouth. Routine bacterial cultures demonstrated only a slight participation of the common pyogenic flora in the ulcerative processes, while other venereal diseases could be excluded by careful laboratory examination. The usual local antiseptic therapy did not influence the steadily progressive character of the ulcerations, which in some cases led to extensive mutilation of the external genitalia. The characteristic presence of Vincent's flora in the discharge and the absence of other demonstrative etiologic agents seemed sufficient proof that the lesions were caused by the group of fusospirochetal organisms. Among 622 patients examined in the diagnostic laboratory for venereal diseases established at the Charity Hospital in New Orleans, thirty-seven cases of primary fusospirochetal infection of the genitalia have been recognized. The Negro race, the male sex (twenty-three cases) and the age groups between 20 and 30 years were most frequently represented in the patients suffering from the infection. Intense local pain and penetrating foul discharge were the principal clinical manifestations. Constitutional symptoms were present in twelve patients and one patient died.

American Review of Tuberculosis, New York

38: 531-650 (Nov.) 1938. Partial Index

Body Section Radiography with Laminagraph in Pulmonary Disease. S. Moore, St. Louis.—p. 538.
Mediastinal and Hilar Angiography in Pulmonary Disease: Preliminary Report. I. Steinberg and G. P. Robb, New York.—p. 557.
Bilateral Artificial Pneumothorax. B. H. Douglas, D. H. Saley and C. J. Stringer, Northville, Mich.—p. 570.
*End Results of Thoracoplasty. L. S. Peters and P. G. Cornish, Albuquerque, N. M.—p. 586.
Pulmonary Emphysema in Tuberculosis. E. Korol, Lincoln, Neb.—p. 594.
Tuberculosis of Thyroid Gland. H. W. Louria and M. R. Louria, Brooklyn.—p. 606.
Unusual Mycobacterial Infections. G. Freeman, Chicago.—p. 612.
Basophilic Erythrocytes in Silicosis. T. A. Neal, Detroit.—p. 629.
*Immunization Against Tuberculosis: Study of Essential Factors. M. I. Levine, P. Vogel and H. A. Rosenberg, New York.—p. 632.

End Results of Thoracoplasty.—To show how few private patients can be traced, Peters and Cornish are able to report on but seventy-eight cases out of a series of more than 300. There were forty patients on whom a complete thoracoplasty was performed, 21 per cent of whom became well (negative sputum and cavity closed) while 54 per cent are dead. All these patients were hopelessly ill and would ultimately have died had it not been for the surgical intervention. None were able to work even part time. The others are living with positive sputum and open cavity no better than before operation and will ultimately die of tuberculosis. There were thirty-eight patients on whom a partial thoracoplasty was done, 50 per cent of whom are well (cavity closed and sputum negative) and 34 per cent are dead. The others still show positive sputum, open cavity and inability to work. They too will no doubt die of tuberculosis, but had thoracoplasty not been done all would have died of their disease. The indications for thoracoplasty are about the same as for pneumothorax. These end results, as well as others reported in the literature, prove that all patients who must otherwise die of their tuberculosis should be given the benefit of thoracoplasty if they offer a fighting chance for recovery. To do less is to sacrifice lives that might otherwise be saved. All those reported well have been so for from two to fifteen years.

Immunization Against Tuberculosis.—During the last eleven years a study on the efficacy of BCG vaccination against tuberculosis in children has been carried on in New York City by the Bureau of Laboratories of the Department of Health. Levine and his colleagues report on the methods used up to April 1, 1937, during which time 1,830 children of tuberculous families have been followed, of which 880 were vaccinated and 950 served as controls. In the course of these eleven years of study the importance of selecting adequate controls has been emphasized repeatedly. At the outset of the study an attempt was made to control the experiment by dividing the children into two equal groups, those vaccinated and those not vaccinated. This procedure (usually the children of cooperative parents) was followed from 1926 to Jan. 1, 1933. In all 955 children were studied, 435 of whom were vaccinated, when the procedure of selection was changed so that alternate children were vaccinated and the others served as controls. Under this selection 744 children were observed from Jan. 1, 1933, to Sept. 1, 1936, 383 being vaccinated and 361 held as controls. The results of BCG vaccination before alternate selection was sixteen deaths in the control and three deaths in the vaccinated group. The results of BCG vaccination after alternate selection was instituted was four deaths in the control and six in the vaccinated group. It would seem, therefore, that the manner of selecting cases for vaccination or as controls exerted a marked influence on the final results obtained. A complete study of the participating factors is to be the basis of a forthcoming article.

Archives of Pathology, Chicago

26: 923-1092 (Nov.) 1938

*Carbon Tetrachloride Poisoning: Study of Stages of Hepatic Damage and Repair in Man. T. M. Peery, Washington, D. C.—p. 923
Calcification of Hyaline Cartilage in Man. B. Falconer, Stockholm, Sweden.—p. 942.
*Tissue Reactions to Natural Oils and Fractions Thereof. G. M. Hass, Boston.—p. 956.
Effect of Primary Pulmonary Tuberculous Lesion (BCG) on Experimental Pulmonary Tuberculosis in Rabbits. B. J. Clawson, Minneapolis.—p. 966.
Morphologic Study of Reactivity of Mouse Sarcoma 180 to Bacterial Filtrates. I. E. Gerber and Alice Ida Bernheim, New York.—p. 971.
Effect of Sympathectomy on Vasa Vasorum of the Rat. J. Q. Griffith Jr., C. J. Zinn and B. I. Comroe, with technical assistance of R. Campbell, Philadelphia.—p. 984.
Experimental Gastric Ulcer (Pitressin Episodes). A. J. Nedzel, Chicago.—p. 988.
Pathologic Observations on Adenomatous Lesion of Stomach in Mice of Strain I. H. L. Stewart and H. B. Andervont, Boston.—p. 1009.
Cirrhosis of Liver in Rabbits with Continued Chloroform Poisoning and with Associated Syphilitic Infection. H. W. Ferris, New York.—p. 1023.
Hyperparathyroidism Secondary to Experimental Renal Insufficiency. W. J. Highman Jr. and B. Hamilton, Chicago.—p. 1029.
Case of Primary Reticulum Cell Sarcoma of the Brain: Relationship of Microglia Cells to Histiocytes. C. L. Yuile, Boston.—p. 1036.
Erythroblasts in Chorionic Blood Vessels of Human Embryos. B. Halpert and J. Stasney, New Orleans.—p. 1045.
Metastatic Calcification in a Case of Carcinoma of the Breast. J. W. Egoville, Philadelphia.—p. 1047.

Carbon Tetrachloride Poisoning.—Peery cites three cases of accidental poisoning by carbon tetrachloride in man that have been studied clinically and at necropsy. The deaths resulted from ingestion of a "roach poison" containing a mixture of

carbon tetrachloride and ethylene dichloride, mistaken for an intoxicant. One victim died about eight hours after taking the drug and showed no definite lesions at necropsy. The second died about sixty-eight hours after ingesting the poison and at necropsy acute necrosis of the liver was observed. The third patient died 150 hours after poisoning and at necropsy active regeneration of lost liver cells was seen.

Tissue Reactions to Natural Oils.—In order to determine the reactions of the tissues of experimental animals to oils, Hass injected olive oil and cod liver oil subcutaneously, intramuscularly and intraperitoneally in doses of 0.5, 0.25, 0.1 and 0.05 cc. Old and young animals were used. The tissues were examined at intervals of one, two and three weeks after the injection of each oil. Olive oil persists in an unchanged state in the intercellular medium of the subcutaneous tissues over a period of three weeks. During the same interval cod liver oil is partly transformed into an amorphous homogeneous semisolid material. A part of this material is insoluble in water, alcohol and xylene. Some of the insoluble substance is acid fast. The study of the various fractions of the hydrolyzed oils and the methyl esters of the acid products of hydrolysis shows that the amorphous semisolid material is formed in the intercellular region only in the presence of unsaturated fatty acids or methyl esters of unsaturated fatty acids. An increase in the amount of this material is correlated with an increase in the average unsaturation of the fractions employed. An increase in the intensity of the inflammatory response is associated with an increase in the average unsaturation of the fraction introduced into the tissue spaces. An infiltration with eosinophils is prominent in the zones of reaction to several of the unsaturated fractions in contrast with the relative infrequence of these cells in the zones of reaction to saturated compounds. The numerical distribution of multinucleated giant cells in the regions of response to the unsaturated liquid compounds indicates that the amorphous semisolid material derived from these compounds is the only effective stimulus to giant cell formation. The liquid methyl esters of the saturated acids, in contrast to the glyceryl esters, are rapidly hydrolyzed in the intercellular environment.

Arkansas Medical Society Journal, Fort Smith

35: 105-122 (Nov.) 1938

Diagnosis of Acute Abdomen. G. E. Cannon, Hope.—p. 105.
Hypotension and Its Significance. J. M. Samuel, Little Rock.—p. 108.

Bulletin New York Academy of Medicine, New York

14: 653-710 (Nov.) 1938

*Chemistry and Biology of Male Sex Hormones. F. C. Koch, Chicago.—p. 655.
The Management of Hypertension. H. J. Stewart, New York.—p. 681.

Testis Hormones.—Koch points out that at present six androgens have been found in nature and that four of them have been isolated from human urine. Only androsterone and dehydro-androsterone have been separated from the urine of normal men. Whether all the androgenic activity in these urines resides in these compounds or whether others contribute remains to be determined. Although normal women also excrete large amounts of androgenic material, its exact nature has not been determined. Thus far, pure androgen has not been separated from the urine of normal nonpregnant women. However, in the pregnant woman epiallopregnanolone-3,20 has been separated from the urine as one of the androgens. In pathologic urines there undoubtedly are varying amounts of adrenosterone and pregnanetriol-3,17,20 in addition to androsterone, dehydroandrosterone and many other possible compounds of androgenic character. The normal type of androgen may be increased in concentration in pathologic conditions. In view of the possibilities of complex mixtures existing in various urines in various proportions it is probable that future advances in the quantitative studies on urine will depend to a large extent on the ability to differentiate quantitatively between the different androgens. However, for the present one must be content with the estimation of the total androgenic activity in tissue, body fluids and excretions in attempts to correlate the quantitative information with various endocrine disturbances possibly involving the gonads.

Delaware State Medical Journal, Wilmington

10: 205-222 (Oct.) 1938

The Medical Approach to Sex Instruction in Schools of Delaware. C. J. Prickett, Smyrna.—p. 205.
Industrial Law and the Medical Profession. J. B. McManus, Wilmington.—p. 209.
Treatment of Pneumonia. J. J. Cassidy, Wilmington.—p. 213.

Endocrinology, Los Angeles

22: 535-680 (Nov.) 1938

Oral Administration of Hormone Proteins: Thyroid Protein and Insulin. Hildegarde Wilson, T. S. Sappington and W. T. Salter, Boston.—p. 535.
Effect of Hyperthyroidism on Growth and Chemical Composition of Bone. Evelyn E. Smith and F. C. McLean, Chicago.—p. 546.
Relation of Environmental Temperature to Action of Thyroxine. L. H. Schmidt and Ida Genther Schmidt, Cincinnati.—p. 553.
Variations in Structure of Adrenals and Thyroids Produced by Thyroxine and High Environmental Temperatures. Ida Genther Schmidt and L. H. Schmidt, Cincinnati.—p. 559.
*Syndrome of Infantilism, Congenital Webbed Neck and Cubitus Valgus. H. H. Turner, Oklahoma City.—p. 566.
Influence of Avitaminoses on Weights of Endocrine Glands. B. Sure, Fayetteville, Ark.—p. 575.
Modified and Improved Method for Preparation of Thymus Extract. A. Steinberg, Philadelphia.—p. 581.
Certain Iodine-Reducing Substances of Thymus Extract: Biologic Considerations. L. G. Rowntree, A. Steinberg, N. H. Einhorn and N. K. Schaffer, Philadelphia.—p. 584.
Id.: Chemical Analysis of Extract. N. K. Schaffer, W. M. Ziegler and L. G. Rowntree, Philadelphia.—p. 593.
*Effect of Anterior Pituitary Sex Fraction on Development of Human Uterus. S. A. Payne and E. K. Shelton, Los Angeles.—p. 598.
Hyaline Change in Basophil Cells of Pituitary Body Not Associated with Basophilism. A. D. Ecker, Rochester, Minn.—p. 609.
Comparative Effects of Light Stimulation and Administration of Gonadotropic Hormones on Female Sparrows. G. M. Riley and E. Witschi, Iowa City.—p. 618.
Subclinical Adrenogenital Syndrome. S. J. Glass and H. C. Bergman, Los Angeles.—p. 625.
Insulin Insensitivity: Its Possible Relation to Pituitary Gland. G. Flaum, New York.—p. 630.
Juvenile Adiposogenital Dystrophy: Neurologic and Psychopathologic Aspects: Results of Organotherapy and Psychotherapy. B. Mittelmann, New York.—p. 637.

Infantilism, Webbed Neck and Cubitus Valgus.—Turner believes that infantilism, webbing of the skin of the neck and deformity of the elbow (cubitus valgus) occurring in the same person is unusual and to his knowledge has not been reported previously. The individual signs are perhaps not uncommon. The seven female patients forming the basis of the author's report cannot be classified under the syndrome of Klippel-Feil, Sprengel's deformity or cervical Pott's disease, as the shortening of the neck is merely apparent, due to the webbing, and not real. There is no absence or fusion of the cervical spine in any of these patients. There is some lowering of the hairline on the back of the neck, but no marked limitation of motion. Torticollis, mirror movements, facial asymmetry and other signs and symptoms, such as difficulty in breathing or swallowing, and shortness of breath, are not present. There is no mental retardation. Deformity of the elbow, consisting of an increase in the carrying angle, or cubitus valgus, is constantly present. All of the author's patients present osseous and sexual retardation similar to that associated with hypo-antuitarism, or the Lorain-Levi type of dwarfism. The blood and urine of these patients were entirely within normal limits. Roentgenograms of the skull, cervical spine, elbow, wrist and pelvis revealed no abnormalities with the exception of demineralization and evidence of delayed union of the epiphyses in six patients. Treatment with pituitary growth hormones has been unsatisfactory. There was definite genital development following the administration of the anterior pituitary gonadotropic substance in the two patients treated.

Gonadotropic Substance and Development of Human Uterus.—Payne and Shelton encountered ten women with small uteri (a depth of less than 2 inches) during a period of twelve months. All had some menstrual disturbance when first seen. A gonadotropic extract derived from the anterior pituitary glands of either hogs or sheep was used. Secondary menstrual disturbances occurred in three women of the group: following an acute infection, a change in climate and environment and after a severe nervous shock. The endometrium obtained by biopsy at the beginning of treatment was atrophic

in all patients. Since there was a response to treatment in all but two of the women, it became apparent to the authors that they were dealing not only with a problem of uterine hypoplasia but also with gonadal insufficiency. In seven of the eight women who responded to treatment there was improvement in menstruation and the endometrium became more normal following injections of the gonadotropic substance. Following these injections the endometrium changed to a secretory type in four patients and one other woman became pregnant, suggesting that anterior lobe extracts may have an influence on ovulation. Uterine growth occurred in three patients, the uterine depth increased from 1¼ to 3½, 1⅜ to 3 and 1½ to 2¼ inches respectively in each woman. It is impossible to draw definite conclusions, but it appears that the anterior pituitary elaborates a substance which stimulates the gonads, including an influence on ovulation and in some cases on uterine growth. Uterine development follows its administration.

Illinois Medical Journal, Chicago

74: 385-476 (Nov.) 1938

The Position of the American Medical Association. I. Abell, Louisville, Ky.—p. 407.
The Educational Committee: Its Origin and Work. J. H. Hutton, Chicago.—p. 411.
Subcutaneous Injuries of the Abdomen. F. Christopher, Evanston.—p. 415.
Injuries to the Right Upper Abdominal Quadrant. P. H. Kreuscher, Chicago.—p. 419.
Ruptured Spleen. C. C. Guy, Chicago.—p. 423.
Mosquito Control in Illinois as a Public Health Measure. S. S. Fuller, Riverside.—p. 428.
Symptom Complex of Visceral-Spinal Pain. E. L. Compere, Chicago.—p. 434.
Pneumonectomy for Bronchogenic Carcinoma of the Lung: Report of Successful Case Sixteen Months After Operation. W. E. Adams, Chicago.—p. 442.
*Milk Sickness. G. H. Gowen, Champaign.—p. 447.
Some Practical Suggestions in Control of Venereal Diseases. A. J. Levy, Chicago.—p. 452.
Amaurotic Family Idiocy (Juvenile Form): Report of Two Cases Occurring in the Same Family. H. B. FitzJerrell and B. B. Neuchiller, Dixon.—p. 456.
Stab Wounds of the Cervical Spinal Cord. K. L. Vehe and R. E. Lyons, Chicago.—p. 461.
Consideration of Some Practical Points in the Management of Inflammatory Diseases of Uveal Tract. G. L. Porter, Urbana.—p. 463.
Sulfanilamide: Its Use in General Practice. A. F. Goodyear, Decatur.—p. 469.

Milk Sickness.—Gowen presents a review of the literature on milk sickness or "trembles." This condition is due to trematol, one of the toxic constituents of white snakeroot (Eupatorium urticaefolium). Milk sickness in man and "trembles" in domestic animals are identical. Animals acquire the disease by eating white snakeroot. Man acquires the disease by consuming milk or milk products from animals that have been eating the plant. Pasteurization does not destroy the poisonous properties. Trembles appear only in pastured animals. In every outbreak investigated by the author the animals had been turned into a wooded area, owing to lack of any other means of nourishment. The symptoms of milk sickness most commonly described and seemingly characteristic in order of occurrence are weakness or prostration, pernicious vomiting, severe constipation and epigastric pain. The temperature is characteristically normal or subnormal. Muscular pains are common. There is marked thirst, the urine is scanty, frequently acetone is found, and the breath has a distinct odor of acetone. Flushed cheeks and undue redness of the lips and tongue are not infrequent. Swelling of the tongue is commonly experienced by the patient. In fatal cases, coma and convulsions precede death. In patients who recover, weakness persists for days, weeks or even months, depending on the initial severity of the illness. Seemingly recovered patients may relapse if undue physical exertion is practiced too soon. In the author's twenty-one patients (two died) there was a direct relationship between the quantity of milk or milk products consumed and the severity of the disease. In general, treatment consists of saline purgation, fluids, alkalis by mouth, dextrose intravenously and enemas. The old remedy of brandy and honey finds some basis in the statement of Hardin, who says: "The administration of alcohol causes an ester of trematol to be formed which is less toxic. If the patient becomes overheated before the ester is excreted, a hydrolysis of the ester occurs, liberating the poison."

Journal Industrial Hygiene & Toxicology, Baltimore

20: 497-534 (Oct.) 1938

The Heated Thermometer Anemometer. C. P. Yaglou, Boston.—p. 497.
Use of New Equipment and Helium Gas in a World Record Dive. E. End, Milwaukee.—p. 511.
Can Lead Poisoning Cause Gastric-Duodenal Ulcers? C. Csépai, Budapest, Hungary.—p. 521.
Methemoglobinemia and Its Measurement. D. O. Hamblin and A. F. Mangelsdorff, Bound Brook, N. J.—p. 523.

Journal of Investigative Dermatology, Baltimore

1: 313-398 (Oct.) 1938

Parasitic Skin Diseases of Domesticated Animals and Their Importance to Dermatologists: A Review. H. M. Martin.—p. 313.
Xanthomatosis: III. Cutaneous Xanthoma, Especially in Relation to Disease of Liver. H. Montgomery, Rochester, Minn.—p. 325.
Studies in Experimental Congenital Syphilis and Transference of Immunity from Immune Syphilitic Female Rabbits to Their Offspring. J. E. Kemp and Elsie Mae Fitzgerald, Chicago.—p. 353.
Skin Test in Lymphogranuloma Inguinale: Brief Review and Discussion of Some Possible Causes of Error. W. Frei, New York.—p. 367.
*Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi: Historical Review, Nomenclature and Theories Relative to the Nature of the Disease, with Experimental Studies of Two Cases. S. W. Becker and H. W. Thatcher, Chicago.—p. 379.

Multiple Idiopathic Hemorrhagic Sarcoma.—Becker and Thatcher discuss the various designations and theories of the origin and etiology of Kaposi's sarcoma. The disease is seen predominantly in Italians and Jews. Incidence late in life with the peak at 70 years suggests neoplastic rather than infectious origin. In most cases the lesions have their onset on the lower extremities. Two cases are presented, one of which ended fatally, with true sarcoma formation. The injection of material from a benign lesion into a patient and a rabbit did not cause the formation of a tumor. The most logical explanation of Kaposi's sarcoma is that it is a multicentric benign neoplasm originating in the perithelial tissue from embryonic mesenchymal cells (lymphocytoid cells of Marchand), which results in a type of cell growth unique for the disease. After a period of years, the cells may undergo malignant degeneration, producing true sarcoma, resulting in metastasis and death. Metastasis by way of the lymphatics in contrast to hematogenous metastasis of most nonlymphocytic sarcomas may be construed as evidence of the lymphocytoid origin of the disease.

Journal-Lancet, Minneapolis

58: 465-504 (Nov.) 1938

Diabetes Mellitus and Protamine Zinc Insulin. A. R. Foss, Missoula, Mont.—p. 465.
Management of Squint. G. M. Constans, Bismarck, N. D.—p. 470.
Student Cooperation in Tuberculosis Control. K. Emerson, New York.—p. 476.
*Chronic Recurring Sciatic Pain Due to Protruded Intervertebral Disks. J. G. Love, A. W. Adson and W. M. Craig, Rochester, Minn.—p. 479.
Practical Points in Interpretation of Allergy Skin Tests. A. V. Stoesser and Ruth Greenberg, Minneapolis.—p. 482.
Infant Feeding. F. W. Schlutz, Chicago.—p. 485.
Vitamin D Deficiency in Infancy and Childhood. P. H. Woutat, Grand Forks, N. D.—p. 493.
Prevalence of Positive Wassermann Reaction, with Special Reference to Railroad Employees. W. Hiemstra, Missoula, Mont.—p. 495.

Sciatic Pain from Protruded Intervertebral Disks.—Love and his colleagues believe that many persons who are suffering from persistent or recurrent attacks of sciatic pain are harboring a protruded intervertebral disk, removal of which will result in dramatic relief of the symptoms. Intervertebral disks may be protruded as a result of an accident or of unusual stress or strain, such as lifting a heavy object. Although any one of the disks may be protruded, those most commonly subjected to this accident are in the lumbar region. The fourth and fifth (lumbosacral) disks are most frequently the cause of the patient's disability. The chief symptoms in cases of protrusion of intervertebral disks are root pain. Since the protrusion most often occurs in the lumbar region, the chief complaint is of pain low in the back and of sciatic pain, usually unilateral. On examination, Lasègue's test (raising the

straight leg) is usually positive and often the achilles tendon reflex on the involved side is diminished or absent. Because of the cases in which values for total protein in the cerebrospinal fluid are normal or low, the authors employ a reversed Queckenstedt test, which is helpful in the diagnosis of lumbar protrusions. This test is based on essentially the same principles as the usual Queckenstedt test, except that the increase in intraspinal pressure in the caudal sac is produced by the extradural injection of a 1 per cent solution of procaine hydrochloride whereas in the Queckenstedt test the pressure comes from within, when the return vascular circulation (internal jugular veins) is obstructed. One of the most important results of this test is the patient's reaction to compression of the cauda equina by the extradural solution. In case of a lesion involving one or more roots of the cauda equina, compression of the caudal sac produces excruciating pain in the involved root. If the value for total protein is normal or low, the reversed Queckenstedt test should be positive before the diagnosis of protruded disk is made. The diagnosis is confirmed and the protruded disk is identified by x-ray examination, after subarachnoid injection of 5 cc. of iodized oil between the spinous processes of the third and fourth lumbar vertebrae. If, on x-ray examination, a persistent defect characteristic of protruded disk is noted and if a lesion at that level could account for the patient's pain, surgical removal of the protruded portion of the disk is indicated. The operative procedure consists of laminectomy and removal, either extradural or transdural, of the protruded portion of the disk. The iodized oil is removed at the time of laminectomy. Fixation of the spine is not necessary. In more than 150 cases the authors have not found it necessary or advisable to perform fusion. The patients are treated postoperatively as if they had undergone simple laminectomy for tumors of the spinal cord. They are kept in bed twelve days and are allowed to leave the hospital on the fourteenth day and to return to their homes three weeks following operation. They are advised to refrain from heavy lifting and straining for at least three months.

Journal of Nervous and Mental Disease, New York

88: 569-732 (Nov.) 1938

Olivopontocerebellar Atrophy and Unilateral Involvement of Cranial Nerve Nuclei. C. Davison and I. S. Wechsler, New York.—p. 569.
Psychosurgery: Effect on Certain Mental Symptoms of Surgical Interruption of Pathways in Frontal Lobe. J. W. Watts and W. Freeman, Washington, D. C.—p. 589.
Pathology of Huntington's Chorea. T. T. Stone and E. I. Falstein, Chicago.—p. 602.
Psychosomatic Relationships in Pruriginous Lesions. H. Kelman and H. Field, New York.—p. 627.
Psychologic Considerations of Insulin Treatment in Schizophrenia. L. L. Orenstein and P. Schilder, New York.—p. 644.

Journal of Pharmacology & Exper. Therap., Baltimore

64: 131-242 (Oct.) 1938

Experiments with an "Antinecrotic" Material Prepared from Liver. H. M. Barrett, D. L. MacLean and E. W. McHenry, Toronto.—p. 131.
Effect of Alarm Reaction on Absorption of Toxic Substances from Gastrointestinal Tract. H. Selye, Montreal.—p. 138.
Trypanocidal Activity and Arsenic Content of Cerebrospinal Fluid After Administration of Arsenic Compounds: II. F. Hawking, T. J. Hennelly and W. T. Wales, with assistance of W. Chinnick; appendix by R. E. Barrett, Cardiff, Wales.—p. 146.
Spirocheticidal Action of Arsphenamines on Spirochaeta Pallida in Vitro. H. Eagle, Baltimore.—p. 164.
Action of Sympathomimetic Amines on Heart-Lung Preparation. J. M. Crismon and M. L. Tainter, San Francisco.—p. 190.
Hydrolysis of Homatropine and Atropine by Various Tissues. F. Bernheim and Mary L. C. Bernheim, Durham, N. C.—p. 209.
Effect of Autonomic Hormones on Thyrotoxic Heart. B. Wise and H. E. Hoff, New Haven, Conn.—p. 217.
*Anesthetic Effects of Chlorine Derivatives of Cyclopropane. V. E. Henderson, Toronto.—p. 225.
Studies on Cholinesterase Activity: I. Manometric Method of Assaying Cholinesterase Action. M. Rinkel and M. Pijoan, Boston.—p. 228.
Studies of Morphine, Codeine and Their Derivatives: XIII. Clinical Study of Comparative Effects of Dihydroisocodeine and Codeine. L. F. Davenport, Boston.—p. 236.

Anesthetic Effects of Cyclopropane.—By experimenting on a rabbit and cats, Henderson found that both monochlorocyclopropane and dichlorocyclopropane are not suitable for anesthesia, as they cause irritation of the lungs. Cats forced to full saturation with cyclopropane take up large quantities of gas, certainly more than 100 cc. per kilogram, and in some cases at least 150; similarly animals receiving methyl cyclopropane absorbed, under similar conditions, equal amounts in spite of its greater anesthetic potency. The evidence from the chlorinated cyclo compounds strongly suggests that substituted cyclopropanes are unstable in the body.

Journal of Urology, Baltimore

40: 467-550 (Oct.) 1938

Tumor of Medulla of Adrenal (Adrenal Pheochromocytoma) with Removal and Relief of Paroxysmal Hypertension. D. W. MacKenzie and D. McEachern, Montreal.—p. 467.
Renal Tumors: Review of 130 Cases. H. M. Soloway, Chicago.—p. 477.
Perirenal Fibrosarcoma. H. H. Howard and H. I. Suby, Boston.—p. 491.
Pelvic Kidney and Renal Vessels in a Newborn Child. G. A. Boylston and R. J. Anson, Chicago.—p. 502.
Spontaneous Rupture of Tuberculous Bladder. T. E. Wyatt and H. L. Douglass, Nashville, Tenn.—p. 506.
Why Are Abnormal Cystometrograms Obtained in Normal Patients? M. L. Boyd and W. A. Smith, Atlanta, Ga.—p. 513.
Dilatation of Contracted Bladder: New Instrument. W. M. Kearns, Milwaukee.—p. 519.
Carcinoma of Prostate with Metastasis in Testis. J. H. Semans, Baltimore.—p. 524.
Metastases from Occult Carcinoma of the Prostate. O. S. Culp, Baltimore.—p. 530.
Testicular Tumors in Dogs. C. F. Schlotthauer, J. R. McDonald and J. L. Bollman, Rochester, Minn.—p. 539.

Kansas Medical Society Journal, Topeka

39: 413-456 (Oct.) 1938

Hoarseness. H. W. Powers, Topeka.—p. 413.
Pyogenic Osteomyelitis of the Pelvis: Analysis and Discussion of a Single Case. R. C. Jeffries, Atchison.—p. 417.
Essential Hypertension and Cardiovascular Disease. A. Arkin, Chicago.—p. 418.
Diagnostic Errors in the Field of Internal Medicine. J. M. Porter, Concordia.—p. 420.

Laryngoscope, St. Louis

48: 615-698 (Sept.) 1938. Partial Index

The Management of Cancer of the Nasal Sinuses. M. C. Myerson, New York.—p. 615.
Chronic Frontal Sinusitis: A New Endonasal Surgical Approach. F. E. Stone and M. Berger, Brooklyn.—p. 626.
Treatment of Laryngeal Carcinoma. R. Kramer, New York.—p. 645.
The Art of Good Tone Production, with Some Helpful Suggestions. H. A. Schatz, Philadelphia.—p. 656.
Tetanus Associated with Acute Otitis Media; Probable Atrium Tetanus: Report of Two Cases. P. S. Stout, Philadelphia.—p. 682.

48: 699-764 (Oct.) 1938

*Use of Estrogenic Substances in Atrophic Rhinitis. I. H. Blaisdell, Boston.—p. 699.
Concussion Sound Waves from Large Guns in Action: Author's Abstract. D. C. Miller, Cleveland.—p. 720.
Diseases of Maxillary Sinus and Their Relationship to Oral Cavity. J. M. Loré, New York.—p. 724.
Modification of Semilunar Ganglion Approach Used in Surgery of Petrous Pyramid. M. F. Jones, New York.—p. 738.
Sarcoma of Larynx. I. Arons, New York.—p. 745.
Tuberculous Tonsillitis: Clinical-Pathologic Study Based on 782 Tonsillectomies. J. H. Abronheim, Jackson, Mich.—p. 749.
The Crooked Nose. A. A. Cinelli, New York.—p. 760.

Estrogen in Atrophic Rhinitis.—Blaisdell states that estrogenic substances were first used in cases of atrophic rhinitis in the outpatient department of the Eye and Ear Infirmary on Aug. 1, 1937. A series of sixty cases is presented, divided into two groups; group 1 consists of patients with an onset (true atrophic rhinitis) before 20 years of age and group 2 is made up of patients with onset (secondary atrophic rhinitis) of symptoms after 20 years of age. There was clinical improvement, as shown by diminution of crusts and odor in 86.4 per cent of the patients in group 1 and improvement of all patients in group 2. Because of its wide variety of effects on the body, aside from its function as a sex hormone, estrogen, properly used, is one of the greatest weapons for combating diseases and physiologic conditions which heretofore have been obscure. Besides acting as a hormone estrogen acts also like a drug and its action is farther reaching than insulin, more powerful than epinephrine and more spectacular than ergot. As the study of this substance progresses, its exact place in the armamentarium of the otolaryngologist will undoubtedly be found. The relationship

between menstrual abnormalities and atrophic rhinitis should be undertaken by a gynecologist. The exact mechanism by which estrogen acts on the nose is not known and the extent of changes in the mucosa, as well as the permanence of the improvement clinically, can be determined only after years of carefully studying these cases.

Nebraska State Medical Journal, Lincoln

23: 401-440 (Nov.) 1938

Anterior Pituitary-Gonad Relationship in the Female with Clinical Application. A. A. Werner, St. Louis.—p. 401.
Hospital Insurance. C. C. Johnson, Lincoln.—p. 404.
Specificity of Methods for Determining Concentration of Ethyl Alcohol in Body Fluids with Specific Reference to the Heise Method. D. F. Bavis and M. F. Arnholt, Lincoln.—p. 407.
Further Standardization After Experience with Injection Treatment of Hernia. L. E. Hanisch, Omaha.—p. 413.
Analysis of 186 Consecutive Ambulatory Cases of Heart Disease. E. Thompson, Omaha.—p. 415.
Pneumatic Lift for Gallbladder and Kidney Operations. H. S. Andrews and B. B. Sutton, Minden.—p. 419.
Bone Marrow Biopsy. J. P. Tollman, Omaha.—p. 421.
Socialized Medicine in Sweden. P. Findley, Omaha.—p. 425.

New England Journal of Medicine, Boston

219: 635-684 (Oct. 27) 1938

Reported Gonorrhea and Syphilis in Massachusetts, 1930-1937. E. B. Howard, Boston.—p. 639.
Opportunity for Modern Treatment of Lobar Pneumonia in General Practice. H. D. Levine, Bristol, N. H.—p. 644.
Cold as a Standard Stimulus of Blood Pressure: Study of Normal and Hypertensive Subjects. D. Ayman and A. D. Goldshine, Boston.—p. 650.
Human Autonomic Pharmacology: XIX. Effect of Mecholyl, Prostigmine, Benzedrine Sulfate and Atropine on Urinary Tract: Urographic Studies. J. Lieman, B. Greenberg and A. Myerson, Boston.—p. 655.
Activation of Peritoneal Mechanism of Defense. H. L. Johnson, Boston.—p. 661.

New York State Journal of Medicine, New York

38: 1369-1426 (Nov. 1) 1938

*Type I Pneumococcus Pneumonia: Observations from Study of 2,000 Cases Treated with Specific Serum. E. S. Rogers and Marjorie E. Gooch, Albany.—p. 1369.
Syphilis: Chance of Acquisition and Frequency of Its Disastrous Course. R. A. Vonderlehr and Lida J. Usilton, Washington, D. C.—p. 1376.
Serodiagnosis of Infectious Disease. A. B. Wadsworth, Albany.—p. 1383.
Fractures in the Small Hospital, with Observations on Common Sources of Error and Fundamentals and Psychology of Treatment. R. F. Sengstacken, Suffern.—p. 1387.
Thrombocytopenic Purpura: Nonsurgical Treatment. H. M. Greenwald, Brooklyn.—p. 1391.
Some Toxic Manifestations Following Use of Sulfanilamide. D. Greenberg, New York.—p. 1394.
Spontaneous Rupture of Splenic Artery. A. Segal, Brooklyn.—p. 1396.
Retrograde Intussusception of Cecum into Ileum. E. S. Goodyear, Kingston.—p. 1397.
Slit Lamp Principle: Its Use as Simple Aid to Inspection in Physical Diagnosis. N. E. Reich, Brooklyn.—p. 1398.
Contact Implantation of Cancer: Carcinoma of Lower and Upper Lips. H. Charache, Brooklyn.—p. 1400.

Type I Pneumococcus Pneumonia.—During a period of twenty-five months 2,293 cases of type I pneumococcus pneumonia occurred in New York State exclusive of New York City. Rogers and Gooch discuss the 2,027 cases that were treated with concentrated type I antipneumococcus horse serum. Age had a direct influence on prognosis in the patients treated with serum as well as those not treated with it. Sex apparently influences morbidity but not mortality, save through its relationship to pregnancy. The data suggest that pregnancy may prove to be a factor predisposing to pneumonia and that the last four months of pregnancy most seriously influence the prognosis. The seriousness of bacteremia as reported by many other observers has been corroborated. The mortality rises in direct relation to the duration of the disease at the time treatment is started. Among 544 patients treated on or before the fourth day of illness the fatality rate was 15.8 per cent, as contrasted with 33.9 per cent for 183 patients receiving treatment later than on the fourth day of illness. Of the 544 patients, 251 received less than 100,000 units of serum and 17.5 per cent of them died; 293 received 100,000 units or more and 14.3 per cent of them died. This does not offer impressive evidence in favor of large dosage. However, if the group of 293 patients is further analyzed it is found that only sixty-six of them received what might be termed "intensive" treatment, that is to say received all their serum within a period of twenty-four hours. Of these sixty-six patients only 6.1 per cent died, while of the 227 patients who received a similar amount of serum over more than twenty-four hours, 16.7 per cent died. The use of type I serum in the treatment of improperly typed cases, untyped cases or cases of heterologous types is discouraged. Of 129 such reports (not included in the 2,027 patients in the present series) the crude case fatality rate was 28.6 per cent.

Northwest Medicine, Seattle

37: 307-342 (Oct.) 1938

Urgent Medical Problems. J. R. Morrison, Bellingham, Wash.—p. 312.
Principles Which Should Govern the Therapeutic Use of Sulfanilamide. E. E. Osgood, Portland, Ore.—p. 314.
Gastrectomy for Gastroduodenal Ulcer. E. C. Moore, Los Angeles.—p. 318.
Gas Distention of the Appendix in Acute Appendicitis: Case Report. B. N. Wade, Portland, Ore.—p. 323.
Treatment of Threatened and Habitual Abortion: Report of Two Cases. W. R. Frazier, Portland, Ore.—p. 324.
Symptoms of Early Malignancy of Upper Air Passages. I. E. Gaston, Portland, Ore.—p. 326.

Philippine Islands Med. Association Journal, Manila

18: 549-616 (Sept.) 1938

Tuberculosis: A Public Health Problem in the Philippines Which Requires Development of Balanced National Tuberculosis Program. S. A. Francisco, Manila.—p. 549.
Ectopic Pregnancy. H. Acosta-Sison and J. S. Galang, Manila.—p. 557.
Multiple Serositis: Report of Case. A. B. M. Sison, Manila.—p. 565.

Psychoanalytic Quarterly, Albany, N. Y.

7: 299-420 (July) 1938

Psychoanalysis Comes of Age. F. Alexander, Chicago.—p. 299.
Folie à Deux. Helene Deutsch, Boston.—p. 307.
Akinesia After Ventriculography: Contribution to Ego Psychology and the Problem of Sleep. M. Grotjahn and T. M. French, Chicago.—p. 319.
Telepathic Sensitiveness as a Neurotic Symptom. L. J. Saul, Chicago.—p. 329.
Incidental Observations on Pruritus Ani. L. J. Saul, Chicago.—p. 336.
Incidence and Character of Masturbation Threats in a Group of Problem Children. Mabel Huschka, New York.—p. 338.
A Paranoid Mechanism in Male Overt Homosexuality. L. N. Bollmeier, Hot Springs, Ark.—p. 357.
The Psychogenesis of a Fatal Organic Disease. B. Berliner, San Francisco.—p. 368.

Southern Medical Journal, Birmingham, Ala.

31: 1117-1218 (Nov.) 1938

Cysts of the Kidney. E. R. Whitmore, Washington, D. C.—p. 1117.
Wilms' Tumors. G. W. Reagan, Little Rock, Ark.—p. 1129.
Congenital Valves of Posterior Urethra: Report of Case Associated with Spina Bifida Occulta and Vesical Diverticulum. Emma S. Moss and J. R. Schenken, New Orleans.—p. 1134.
*Acute Streptococcic Lung Abscess Treated with Sulfanilamide: Case Report. F. B. Murphey Jr. and J. M. Frere, Chattanooga, Tenn.—p. 1136.
Treatment of Skin Cancer. E. C. Fox, Dallas, Texas.—p. 1139.
Evolution of Radiation Therapy for Carcinoma of Cervix Uteri, with Special Reference to Methods Used at Roper Hospital. B. Kalayjian and H. Rudisill Jr., Charleston, S. C.—p. 1143.
Diagnostic Bronchoscopy. J. S. Agar, Little Rock, Ark.—p. 1150.
Treatment of Pellagra with Nicotinic Acid: Observations in Forty-Five Cases. V. P. Sydenstricker, H. L. Schmidt Jr., M. C. Fulton, J. S. New and L. E. Geeslin, Augusta, Ga.—p. 1155.
*Further Observations on Effect of 2,6-Dimethyl Dinicotinic Acid and Dinicotinic Acid on Pellagrins in Relapse and on Normal Persons. Sue Potter Vilter, W. B. Bean and T. D. Spies, Cincinnati.—p. 1163.
Convulsive Therapy in Mental Disorders. N. M. Owensby, Atlanta, Ga.—p. 1164.
Prophylactic Use of Pertussis Vaccine (Sauer): Report of Results in Private Practice. C. Howell, Baltimore.—p. 1166.
Meningococcic Meningitis: Observations in 157 Cases in the Louisville City Hospital. T. C. Smith, Louisville, Ky.; W. T. Maxion, Lexington, Ky., and D. F. H. Murphey, Louisville, Ky.—p. 1168.
Elliott Therapy of Pelvic Inflammations in the Negress. G. A. Williams, Atlanta, Ga.—p. 1171.
Syringe Adaptor for Rectal Use. M. H. Prosperi, Washington, D. C.—p. 1174.

Lung Abscess Treated with Sulfanilamide.—Murphey and Frere successfully treated a case of abscess of the lung caused by the hemolytic streptococcus with sulfanilamide. They believe that the use of the drug in their case caused immediate symptomatic and clinical improvement and perhaps

shortened the duration of the disease. When hemolytic streptococcus infection is found in the acute stage of pulmonary suppuration sulfanilamide is worthy of trial, provided no contraindications exist.

Dinicotinic Acid in Pellagra in Relapse.—Vilter and her associates used dimethyl dinicotinic acid (2,6-dimethylpyridine-3,5-dicarboxylic acid) or dinicotinic acid (3,5-pyridine dicarboxylic acid) in treating nine pellagrins in relapse and two nonpellagrous persons. These patients received orally from 500 to 1,000 mg. of the acid daily. Each acid, although soluble with difficulty, was completely dissolved in water before administration. The nine pellagrins were severely ill. Some temporary improvement was observed in five of the patients, the response being characterized by an increased feeling of well-being and a partial decrease in the fiery redness of the tongue. The subsequent administration of nicotinic acid, however, elicited a more complete response. The physiologic response to these drugs was quite different from the response to nicotinic acid. Neither oral nor intravenous administration has been found to produce the flushing reaction and rise in cutaneous temperature which occur after similar doses of nicotinic acid. Observations show that 2,6-dimethyl dinicotinic acid and dinicotinic acid have only a partial beneficial effect on pellagra in relapse and they should not be used as a substitute for nicotinic acid. The authors feel that protein deficiency in pellagra is of more importance in the syndrome of pellagra than is currently stressed and that perhaps a close interrelationship exists between protein metabolism and the role of nicotinic acid. At any rate a well balanced high caloric diet should be administered simultaneously with the nicotinic acid.

Texas State Journal of Medicine, Fort Worth

34: 391-454 (Oct.) 1938

Earlier Recognition of Intra-Abdominal Malignant Lesions. W. Walters, Rochester, Minn.—p. 397.
Patent Urachus. H. Dudgeon Jr., Waco.—p. 401.
Treatment of Gas Gangrene Infections. J. J. Faust, Tyler.—p. 404.
*Comparative Study of Foille with Tannic Acid and Tannic Acid Preparations in Treatment of Burns. T. C. Terrell, Fort Worth.—p. 409.
Recent Advances in Hematology. E. E. Osgood, Portland, Ore.—p. 416.
Thrombocytopenic Purpura. D. Neighbors, Fort Worth.—p. 419.
Anemia in the Aged (Syndrome of Kyphosis, Gastric Hernia and Anemia). H. M. Winans, Dallas.—p. 422.
Study of Children Born of Positive Reactor Tuberculous Mothers. E. A. Wright, Houston.—p. 424.
Diethylene Glycol Poisoning: Report of Case with Necropsy Findings. P. Brindley and M. P. Kelsey, Galveston.—p. 426.
The Ultraviolet Ray as an Eye Hazard. V. D. Rathgeber, Fort Worth.—p. 431.
Nasal Physiology and Its Relation to Sinus Surgery. J. M. Robison, Houston.—p. 434.

Comparison of Preparations Used for Treating Burns.—Terrell gives the composition of foille (0.14 per cent of potassium iodide, 0.25 of calcium iodide, 0.39 of calcium soap, 0.02 of calcium thiosulfate, 0.086 of calcium sulfite, 0.1 of oxyquinoline sulfate, 1.4 of ethyl alcohol by volume, 2.8 of phenol, 1.3 of ethyl aminobenzoate, 3.4 water, 90.11 of vegetable oil and sulfur and glycerin present) used in the prolonged treatment of burns. It is not toxic nor does it cause any detrimental systemic reactions. Its formula has been clinically tested with reference to analgesic, antiseptic and healing properties. Dogs have been used for experimental purposes. It has been used on human patients to a sufficient extent to warrant its recommendation in the treatment of all recent wounds and burns. It has been found safe to use in extensive as well as minor burns. The preparation has been tested on several occasions and found to have a low phenol coefficient, but in spite of this and its phenol content it has been proved that it is not injurious to the tissues when used in concentrated form. A thick layer of the medication is applied and a sterile dressing is placed over the wound. The wound is kept constantly bathed with the emulsion for forty-eight hours; then the dressing is removed and the preparation is reapplied. Thereafter, two or three applications are required each day until healing is complete. Experimentally, the burns of dogs treated with it healed much more rapidly and with considerably less discomfort than those treated with 10 per cent tannic acid or with either of two proprietary tannic acid preparations. The preparation offers a much shorter convalescence to the patient, with more comfort and less scarring, without the danger of toxic manifestations.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Children's Diseases, London

35: 165-240 (July-Sept.) 1938

Exophthalmic Goiter in Children. F. R. B. Atkinson.—p. 165.
Treatment of Diphtheria and Scarlet Fever by Active Immunization. K. Sedláček.—p. 175.
Congenital Cardiac Pentad: Fallot's So-Called Tetralogy Together with Common Interventricular Orifice. W. M. Feldman and Sheila G. Snook.—p. 183.
Morbilli Bullosi: Report of Fatal Case. E. James and A. A. Miller.—p. 191.

British Journal of Experimental Pathology, London

19: 273-366 (Oct.) 1938

Antigenic Differences in Strains of Epidemic Influenza Virus: I. Cross Neutralization Tests in Mice. T. P. Magill and T. Francis Jr.—p. 273.
Id.: II. Cross Immunization Tests in Mice. T. Francis Jr. and T. P. Magill.—p. 284.
Serologic Races of Influenza Virus. W. Smith and C. H. Andrewes.—p. 293.
Rate of Absorption of Carcinogens and Local Tissue Reaction as Factors Influencing Carcinogenesis. P. R. Peacock and S. Beck.—p. 315.
Failure of Acute and Subacute Inflammation to Influence Carcinogenesis with 3: 4-Benzpyrene. S. Beck.—p. 319.
Susceptibility of Voles to Human and Bovine Strains of Tubercle Bacilli. A. O. Wells.—p. 324.
Specific Character of Stage of Aggregation in Agglutination and Precipitation of Antibody-Antigen Compounds. J. T. Duncan.—p. 328.
*Microscopic Observations on Bacteriophage of Bacterium Coli. K. B. Merling-Eisenberg.—p. 338.
Functional Hyperplasia of Parathyroids in Experimental Anemias. A. B. Eisler.—p. 342.
Role of Adrenal Gland and of Raised Metabolism in Production of Organ Hypertrophy in Thyroid-Fed Rat. O. L. V. S. de Wesselow and W. J. Griffiths.—p. 347.
Study of Experimental Immunity to Virus of Psittacosis in the Mouse, with Special Reference to Persistence of Infection. S. P. Bedson.—p. 353.

Bacteriophage of Bacterium Coli.—The studies performed by Merling-Eisenberg demonstrate the particulate nature of the bacteriophage of Bacterium coli. They point in the same direction as experiments of Elford, Andrewes and Tang (1936) and of McIntosh and Selbie (1937), who have shown by centrifugation that the bacteriophage action is bound to an agent of particulate nature. Because of their small size the bacteriophage bodies are not visible in transmitted light or stained preparations, which were the methods used by Wollmann (1925). d'Herelle (1926) has not observed any motion of the bodies within the bacterial cells, and he also reports only between fifteen and twenty-five bodies released from one bacterium. This is no doubt due to the optical system which he has employed. It obviously enabled him to perceive only the coarser granulate disintegration of the membrane into from fifteen to twenty-five particles, but not the ten times greater number of the much fainter bacteriophage bodies. The bacteriophage is distinguished from non-specific particles and its size is found to be 25 millimicrons.

British Medical Journal, London

2: 875-928 (Oct. 29) 1938

States of Depression: Their Clinical and Etiologic Differentiation. A. Lewis.—p. 875.
*Clinical Significance and Estimation of Blood Vitamin B1. E. N. Rowlands and J. F. Wilkinson.—p. 878.
Treatment of Brucella Abortus Infection with Fuadin and Prontosil. A. P. Thomson.—p. 884.
Report on Five Cases of Brucella Abortus Infection. M. Gaffney.—p. 885.
*Suppression of Lactation by Oral Estrogen Therapy. G. L. Foss and P. Phillips.—p. 887.

Significance of Blood Vitamin B_1.—Rowlands and Wilkinson established that the phycomyces test, based on Schopfer's discovery (1935) that the growth of the mold Phycomyces blakesleeanus was proportional within certain limits to the amount of vitamin B_1 present in the medium, is a fairly reliable method of estimating vitamin B_1. They determined the standard range for normal blood, taken from healthy members of the departmental staff, who gave figures ranging between 6.5 and 16.5 micrograms per hundred cubic centimeters of blood. Estimations were also carried out on a series of patients suffering

from alcoholic neuritis, nonalcoholic polyneuritis, subacute combined degeneration, diabetic neuritis, nutritional neuritis, anemias, and cardiovascular, renal and endocrine diseases. The investigations seem to show that gross vitamin B_1 deficiency is rare in England. This is not unexpected, since the daily requirement for the normal person is about 500 international units (1 mg. of pure vitamin B_1): vitamin B_1 has a very wide distribution in foodstuffs and it is therefore almost impossible for the intake to be inadequate with a reasonable diet. This is in contrast to the position with vitamin C, the distribution of which is restricted to certain types of food. Nevertheless, vitamin B_1 deficiency may arise from an inadequate supply, inadequate absorption, inadequate utilization or through its destruction in the alimentary tract. In many of these deficiencies an inadequate dietetic intake leads to anatomic or physiologic changes within the intestine and then to diminished absorption, which in turn leads to further disorder of the intestinal function. Moreover, some balance between the specific nutritional elements, such as iron and vitamin B_1, may be necessary. The only conditions in which a gross deficiency of vitamin B_1 was found were alcoholic neuritis, nutritional neuritis, scurvy and malnutrition. In these cases definite improvement followed the administration of vitamin B_1 (and vitamin C in the scorbutic patient). A partial deficiency was observed in simple achlorhydric anemia. The cases of subacute combined degeneration of the spinal cord gave normal figures; therefore the poor therapeutic results following the administration of vitamin B_1 obtained by workers in this field are not surprising. Similarly, the vitamin has not proved of much value in polyneuritis other than the alcoholic, gestational and nutritional forms. This observation corresponds with the values for blood vitamin B_1 found in this series. It appears, therefore, that the changes in the nervous system in these conditions, though clinically similar to those reported in beriberi, have a different etiology and are not associated with vitamin B_1 deficiency. There is no clinical evidence that vitamin B_1 is concerned in hemopoiesis, and this is corroborated by the normal figures given by this test in the uncomplicated primary anemias.

Suppression of Lactation by Oral Estrogen Therapy.—Foss and Phillips state that experience in a few cases of acromegaly and thyrotoxicosis when attempting to inhibit the function of the anterior pituitary in human beings (Foss, 1937), together with Zondek's statement (1936) regarding the quantity of estrogen necessary to retard growth and gonadotropic function in rats, makes it difficult to realize that oral theelin in doses of from 20,000 to 30,000 international units given over a period of from two to six days can inhibit a function of the anterior pituitary. Normally this is held in check only by massive amounts of estrogen and/or progesterone in the placenta. It is much more possible, in the authors' opinion, that theelin acts specifically on the mammary gland, in some way preventing the action of the lactogenic hormone of the anterior pituitary or even by direct antagonism. At present an explanation of this clinical observation cannot be ventured. It is unlikely that such small doses will in any way influence the chemical constitution of human milk.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

45:769-892 (Oct.) 1938

Lipoid Rich Granulosa-Cell Tumor with Discussion on Theca-Cell Tumor. J. G. Thomson and F. Stabler.—p. 769.
Treatment of Myoma. P. Werner.—p. 780.
*Value of Urea Clearance Test in Pregnancy. Doris B. Brown.—p. 786.
Dysgerminoma of the Ovary, Associated with Masculinity: Case. A. Gough.—p. 799.
*Human Fetal Electrocardiogram. G. H. Bell.—p. 802.
Duplication of the Hind End of an Anencephalic Fetus. A. E. Harbeson.—p. 810.
Effects of Intravenous Vasopressin on Toxemias of Pregnancy. E. de Valera and R. J. Kellar.—p. 815.
Acute Inversion of the Uterus. J. H. Peel.—p. 821.
Squamous Cell Carcinoma Occurring in an Ovarian Dermoid, with Secondary Involvement of Uterus, Fallopian Tube and Bowel: Case. R. B. Mehlenbeck and J. A. Stallworthy.—p. 830.
A Flying Fetus. R. W. Knowlton.—p. 834.

Urea Clearance Test in Pregnancy.—Brown presents the results of 671 urea clearance tests performed on 243 pregnant women. The urea clearance test was first determined for normal pregnant women and then tests were made both before and after delivery on women with toxemia and on some patients who had pyelitis of pregnancy. A normal clearance test does not necessarily mean a normal kidney, as the test may be normal until from two thirds to three fourths of the renal tissue has been rendered functionless and also the clearance value is influenced by an alteration in the circulation rate and the supply of oxygen to the kidneys so that the results are lowered by severe anemia and cardiac decompensation. A low clearance value in an apparently well patient should be repeated and it must always be kept in mind that variations of less than 20 per cent are of no significance. The clearance results in the present series were less constant after than before delivery. Harrison says that in severe renal damage the clearance is more fixed than in normal persons. Each patient, therefore, must be considered separately. The urea clearance test extends but never replaces clinical investigation. The differential diagnosis between preeclamptic toxemia, chronic nephritis and essential hypertension is made much easier by the urea clearance test. Before delivery a high value excludes chronic nephritis and if the blood pressure remains high with little other evidence of toxemia and a high clearance the case is probably one of essential hypertension. If the clearance is low the result is of no value in pregnancy in the differentiation of preeclamptic toxemia, chronic nephritis and essential hypertension but the result after delivery is of great value—most patients suffering from preeclamptic toxemia show a rapid rise within a week or two of delivery, while in chronic nephritis the percentage rise is much less and the clearance never reaches a normal level. The follow-up of patients shows that if the clearance is high during the toxemia the prognosis is good even if the degree of toxemia is clinically severe, and the same may be said if the clearance rises to more than 100 per cent within a week or so of delivery even if the clinical condition lags behind. The clearance test is of most value several months after delivery when low tests show definite renal damage at a time when clinical signs may be slight or absent, although possibly on repeated clinical examination some evidence may be found in practically all cases. A low urea clearance is sufficient in the author's opinion to forbid a future pregnancy for at least two years, when further clinical examination and the clearance test should be repeated. Stander, Ashton and Cadden think that a urea clearance below 80 per cent is strongly suggestive of renal damage; therefore a further pregnancy is not wise. The clearance test is also useful during the treatment of toxemia; if the test is rising or remaining stationary, conservative treatment can be continued with confidence.

The Human Fetal Electrocardiogram.—Using a thermionic valve electrocardiograph susceptible of high amplification, Bell obtained electrocardiograms when leads were taken from the abdomen of pregnant women which show in some cases waves which are almost certainly fetal in origin. The evidence supporting the fetal origin is that the direction of the fetal deflection depends on the presentation (vertex or breech) and in a case of twin pregnancy two sets of deflections were obtained. Of thirty-three pregnant women examined in the last two months of pregnancy about one third showed positive results, but the other two thirds did not show any wave on the electrocardiogram which could be definitely recognized as fetal. It is suggested that the failure to secure positive results in all the electrocardiograms is due partly to differences in the electrical properties of the abdominal wall and partly to the electrical disturbances produced by the abdominal muscles, and not to insufficient sensitivity of the apparatus.

Lancet, London

2:867-928 (Oct. 15) 1938

Bacteremia. J. A. Ryle.—p. 867.
Treatment of Ankle Fractures. W. G. Campbell.—p. 872.
*Oxygen Therapy, with Note on a New Nasal Mask. R. V. Christie.—p. 876.
A New Chemical Contraceptive. J. R. Baker, R. M. Ranson and J. Tynen.—p. 882.
Cardiazol Convulsion Therapy in Nonschizophrenic Reaction States. L. C. Cook and W. Ogden.—p. 885.

Oxygen Therapy.—Christie states that there are broad principles which must be appreciated if oxygen is to be used with understanding. The first principle concerned is that blood flowing through a healthy lung is more or less completely saturated with oxygen. The second principle is that cyanosis or lack of

oxygen does not cause dyspnea. The relief of dyspnea is of no significance in determining the value of oxygen therapy. The third principle is that if oxygen is given at all it should be given continuously. To give oxygen once every two hours to a patient with bronchopneumonia may be equivalent to placing him on top of Mount Everest and bringing him back to sea level every two hours for a "breather." Most authorities are agreed that the intermittent administration of oxygen is probably worse than useless. Anoxemia can embarrass the heart of a healthy person; therefore the life of a patient with bronchopneumonia or acute pulmonary edema may depend on the efficient administration of oxygen. The indiscriminate administration of oxygen to any patient who is cyanosed and acutely ill is in part responsible for the conflicting evidence on the value of oxygen therapy. Oxygen should be given only when it is reasonable to expect that it will relieve the anoxemia. When cyanosis is due to localized consolidation or to localized collapse of the lung, it can seldom be relieved by oxygen. When cyanosis is due to a generalized impairment of aeration or to an inflammatory process scattered throughout the lung, oxygen, if properly given, should relieve cyanosis. An adequate supply of oxygen is as important as the method used for its administration. The most satisfactory methods for the administration of oxygen are the nasal catheter, the nasal mask and the oxygen tent. The nasal catheter is often too uncomfortable for continuous use if oxygen is given in amounts adequate for an adult. In infants the catheter may be satisfactory. The nasal mask is efficient, comfortable and inexpensive. A nasal mask for oxygen administration is described that combines efficiency with simplicity of operation and assures the comfort of the patient.

Medical Journal of Australia, Sydney

2: 585-626 (Oct. 8) 1938

Symptomatology and Treatment of Bites of Australian Snakes. C. H. Kellaway.—p. 585.
Pirates and Buccaneers. L. Duncan.—p. 589.
Outbreak of Gastro-Enteritis: Suspected Food Poisoning with Milk as a Possible Vehicle. J. Dale.—p. 591.
Consideration of General Anesthesia for Dental Surgery. N. E. Heath. —p. 594.
A Postgraduate Holiday. J. B. Hamilton.—p. 599.

South African Medical Journal, Cape Town

2: 613-654 (Sept. 10) 1938

*Rickettsioses of South Africa. A. Pijper and C. G. Crocker.—p. 613.
A Mountain Stretcher. G. A. P. Ross.—p. 630.
Onyalai: A Form of Purpura Occurring in Tropical Africa: Report of Cases Occurring in South Africa. J. Gear.—p. 632.
Bantu Syphilis. S. V. Humphries.—p. 637.
Amasa. G. G. Hay.—p. 639.
The Position of General Hospitals in South African Health Organization. H. S. Gear.—p. 642.
Note on Anopheles Gambiae Giles and Anopheles Coustani Variety Tenebrosus Donitz from Southern Africa. B. de Meillon.—p. 648.
Heredity in Nervous and Mental Disease. S. Berman.—p. 651.

2: 655-690 (Sept. 24) 1938

The Unholy Triad: Tuberculosis, Venereal Disease, Malnutrition. P. W. Laidler.—p. 658.
Obstetrics: Ancient and Modern. J. A. Lloyd.—p. 666.
Surgical Aspects of Endocrinology. A. G. Sweetapple.—p. 669.
The Medical Aspect of Endocrine Disease. J. S. Alexander.—p. 673.
The Gynecologic Aspect of Endocrine Disease. D. F. Standing.—p. 676.

2: 691-742 (Oct. 8) 1938

Chemoprophylaxis of Malaria in Portuguese India. I. Froilano de Mello. —p. 710.
Wild Animals as Carriers of Infection. G. de Kock.—p. 725.

Rickettsioses of South Africa.—Pijper and Crocker believe that the three South African rickettsioses (tick-bite fever, murine or rat-flea or sporadic typhus and louse typhus) have been insufficiently studied, especially as regards their relationship with rickettsioses of other countries. Cross immunity tests have been performed only between tick-bite fever and spotted fever, with quite negative results, and by means of immune serum it has been shown that tick-bite fever and Rocky Mountain spotted fever probably have little in common. The need for further work in this and other directions is stressed, because there is evidence that the three South African rickettsioses form a group by themselves, possessing closer affinities with one another than with rickettsioses of other countries. The virus of tick-bite fever is not filtrable, does not produce lesions in rabbit's eyes and the authors were unable to cultivate it on the chorio-allantoic membrane. A brief experiment showed that heartwater and tick-bite fever have nothing in common, although the two can be conveyed by the same tick. The contention that South African epidemic typhus is not identical with classic typhus is based on the results of Weil-Felix tests on patients: lower titer of X 19, good agglutination of X 2 in many cases, sometimes agglutination of X K. The authors have now confirmed this serologic difference by studying the agglutinin titers of a large number of rabbits infected with their Basutoland strain of epidemic typhus. In sporadic typhus in South Africa a virus was found that proved to be immunologically identical with a virus in rats. It protected against tick-bite fever but not against epidemic typhus. Epidemic typhus gives protection against this virus, as it does against tick-bite fever. The authors have now studied the agglutinin curves of several cases of this sporadic typhus and confirm in detail previous observations: agglutination of both X 19 and X 2 and sometimes also of X K. This sporadic form of typhus dies out in guinea pigs when brain injections are used; the epidemic form can be kept going indefinitely by this method.

Chinese Medical Journal, Peiping

54: 201-300 (Sept.) 1938

Peking Diets. R. A. Gay and K. S. Yeh.—p. 201.
Foreign Bodies in Urinary Passage. H. E. Shih.—p. 223.
Studies on Control of Fecal-Borne Diseases in North China: VI. Epidemiology of Ascaris Lumbricoides in an Urban Population. G. F. Winfield and T. H. Chin.—p. 233.
Virulence and Immunogenic Activities of Vibrio Cholerae in Preparation of Cholera Vaccine. H. Yü.—p. 255.
*Use of Sodium Carbonate for Concentration of Tubercle Bacilli in Sputum. B. H. Y. T'ang.—p. 259.
Fever Therapy by Electric Means and Its Rationale. H. C. Vassiliadis. —p. 271.
Congenital Cataract. S. Y. Li.—p. 277.

Sodium Carbonate for Concentrating Tubercle Bacilli.—T'ang examined 481 specimens of sputum from patients known to be suffering from pulmonary tuberculosis both by Petroff's 3 per cent sodium hydroxide method and by the sodium carbonate method. (Sodium carbonate in a solution of 7 per cent, allowed to act on the sputum for thirty minutes at a temperature of 65 C., is recommended to replace sodium hydroxide.) Other sputums (132) were examined by the direct smear method made from selected portions of the whole sample before being divided into two portions and further examined by the two concentration methods. It was found that sodium hydroxide concentration revealed only 4 per cent more positive sputums than direct smears, whereas the sodium carbonate method added 26 per cent. Bacilli are found more readily and in larger numbers after sodium carbonate concentration than in direct smears or after sodium hydroxide concentration. A more critical study of established methods of sputum examination was made on five sputums known to contain tubercle bacilli in small numbers. After the preparation of two direct smears from carefully selected particles of the crude sputum, it was divided into four equal portions. One portion of each sputum was treated by one of the four following methods: Pottenger's dilution-flotation, antiformin digestion, Petroff's sodium hydroxide concentration and the sodium carbonate concentration. Two smears of as nearly as possible the same size and thickness were made from each preparation and stained by the Ziehl-Neelsen method. It is probable that actually greater numbers of bacilli were seen after concentration by the sodium carbonate method than after dilution and flotation, as by the former method clumping of bacilli was commonly observed, whereas an even distribution of isolated bacilli was obtained by the latter method. The strongest recommendation for the use of sodium carbonate comes from a consideration that in the year 1936, when sodium carbonate was first used for concentration, the percentage of positive results increased by 7 per cent. During this year there was an increase in the total number of specimens examined. This was not due only to the fact that more patients were being seen but also to repeated examinations of carefully collected specimens of sputum from patients whose sputums were previously reported negative for tubercle bacilli.

Presse Médicale, Paris

46: 1521-1536 (Oct. 15) 1938

Angina Pectoris Is a Unit. V. Audibert and Mlle. Legré.—p. 1521.
*Epilepsy in Cerebral Tumors. J.-A. Chavany and A. Placa.—p. 1522.
Sterility Due Principally to Chronic Gonorrhea. C. Béclère and Elie François.—p. 1525.
Ouabain Arnaud. C. Dimitracoff.—p. 1527.

Epilepsy in Cerebral Tumors.—Chavany and Placa state that epilepsy may appear either in typical or in somewhat abnormal forms during any phase of the clinical evolution of cerebral tumors. On the basis of personal observations in hundreds of cases they encountered it in about 15 per cent of the cases, whereas other investigators give percentages of 21, 30 and even 41. After a brief review of the literature the authors point out that epilepsy can be observed as a secondary sign, connected with ventricular dilatation or cerebral edema, in all forms of cerebral tumors. It appears in three forms: (1) generalized attacks analogous to those of essential epilepsy, (2) abortive (petit) attacks with short loss of consciousness and without convulsive manifestations, and (3) Bravais-jacksonian attacks. Frequent Bravais-jacksonian attacks, which remain similar for months or years, suggest the existence of a cerebral tumor affecting the pyramidal tract in the neighborhood of its origin. Conversely, Bravais-jacksonian attacks that occur less close together (months apart) and perhaps change their aspect suggest, in the absence of the syndrome of intracranial hypertension, an encephalitis and, if an intracranial hypertension exists, they suggest encephalitis or a tumor of extrapyramidal localization. But although in the presence of Bravais-jacksonian attacks that are far apart and polymorphic and are not accompanied by intracranial hypertension the possibility of a cerebral tumor can be excluded, in the presence of numerous and identical Bravais-jacksonian attacks, it is impossible to make a distinction between encephalitis and tumor, since encephalitis may also cause such a clinical picture. The generalized epileptic attacks are often without value for the localization, except that they are often the first sign of a lesion of a mute zone. In case of the abortive (petit) epileptic attacks a temporal localization should be searched for. The Bravais-jacksonian attacks, which have considerable localizing value, constitute often the alarm signal of a compression of the cerebral origins of the pyramidal bundle. The author further calls attention to the considerable prognostic value of epilepsy and particularly of Bravais-jacksonian epilepsy. A long phase of Bravais-jacksonian attacks, more or less close together, and constituting the only symptom, indicates a malignant tumor. However, it is impossible to distinguish only by clinical means an extracortical meningioma from an intraparenchymatous fibrous glioma. On the other hand, Bravais-jacksonian attacks, which are less numerous and which precede, accompany or follow the appearance of a rapidly progressing hemiplegia of the flaccid type, indicate nearly always the existence of a malignant tumor.

46: 1553-1568 (Oct. 22) 1938

Treatment of Anginal Syndromes by 883 F (Diethylaminomethyl-Benzodioxane). A. Clerc, J. Sterne and J.-P. Lenoir.—p. 1553.
*Behavior of Denervated Adrenal Medulla. H. Hermann.—p. 1554.
*Repeated Perforations of Gastroduodenal Ulcers (Description of Two Unreported Cases). J. Gosset, M. Jounneau and J. Allamand.—p. 1556.

Denervated Adrenal Medulla.—For three years Hermann and his collaborators have made studies on the denervated adrenal medulla. In this report he summarizes the results which are of interest in connection with the surgical treatment of arterial hypertension or of diabetes. The investigations revealed that, after the total resection of the secretory nerves of the adrenal medulla in dogs, this gland retains an important part of its functional properties. Its microscopic structure remains normal; it does not lose the power to elaborate its specific product, which is always detected in it in considerable amounts but in smaller quantities than in the tested capsules. The epinephrine thus stored is perfectly mobilizable either by direct electrical excitation of the chromaffin tissues or by pharmacologic agents possessed of epinephrine-secreting powers. Finally the denervated gland secrets in the chloralosed animal, and under the conditions of suprarenojugular anastomosis, minimal quantities of the sympathomimetic hormone. All these observations establish the fact that the adrenals can escape from the control of the central nervous system without losing their capacity to produce and secrete epinephrine. It demonstrates its autonomic functioning and justifies the analogy between the epinephrinogenic gland and the sympathetic ganglion. The author thinks that these experimental observations deserve to be taken into consideration by those who are interested in the surgical treatment of hypertension or of diabetes by means of the denervation of the adrenals or by means of splanchnicectomy.

Repeated Perforations of Gastroduodenal Ulcers.—Gosset and his associates say that in view of the rarity of reports on repeated perforations they were at first under the impression that this is an exceptional accident. After describing the clinical histories of two patients with repeated perforations, whom they recently observed, the authors say that in the literature of recent years they have found sixty-four cases of repeated perforations of gastric or duodenal ulcers, disregarding of course the perforations of postoperative jejunal ulcers, which are comparatively frequent. They admit that they are unable to estimate, even approximately, the incidence of repeated perforation but point out that Pearse observed thirty-three repeated perforations among 4,183 cases of perforated ulcers (about one in 145 cases). Other authors observed two in 227 cases, one in 120, one in seventy-eight, two in ninety and four in eighty-two. These figures indicate that this complication is far from being exceptional. Discussing the pathogenesis of repeated perforations, the authors point out that it has been suggested that they are especially frequent after simple sutures. However, others have shown that this can be explained by the fact that simple suture is the method most frequently employed in the treatment of the first perforation and that on the whole the percentages correspond to those of the diverse technics employed. Regarding the seriousness of the repeated perforations the authors say that it is estimated diversely by different authors, some considering it as extremely grave and others as more benign than the first perforation. Pearse, for instance, reports a mortality as 9 per cent for the repeated perforations as compared to 27 per cent for the primary perforations. To explain the latter figures it has been suggested that the peritoneum developed a sort of local immunity after the first perforation. Discussing the treatment in cases of repeated perforations, the authors say that it does not differ from the usual treatment of perforated ulcers. The choice of the method is determined less by the repetitious character of the perforation than by the size, the location and the callosity of the orifice. The authors think that in selecting the method the surgeon should take into account especially the tenacious character of the ulceration, which is the cause of the repeated perforation. They think that in repeated perforation either gastrectomy should be done immediately or a simple method should be chosen which is least likely to interfere with a subsequent gastrectomy.

Strasbourg Médical

98: 303-318 (Aug. 5) 1938

Results of Treatment of Puerperal Infection by Neoarsphenamine. J. Kreis.—p. 303.
*Treatment of Hypogalactia by Ultraviolet Rays. M. Pelletier.—p. 314.

Treatment of Hypogalactia by Ultraviolet Rays.—Pelletier reports the histories of three women in whom irradiation of the breasts with ultraviolet rays proved effective against hypogalactia, after galactagogue medications had been tried without appreciable results. Following a description of the cases, the author says that this irradiation of the breasts with ultraviolet rays was first recommended in 1924. He applies gradually increasing doses every other day, the irradiations lasting from two to thirty minutes. The maximum number of irradiations is fifteen, followed by maintenance irradiations twice a week for about a month. During the irradiation, petrolatum is applied to the mamilla. The case histories indicate that the distance from the lamp to the breasts is from 60 to 70 cm. The author does not think that the results obtained with the ultraviolet irradiation are due merely to autosuggestion but assumes with some of the earlier investigators that the irradiation counteracts a disturbance in the calcium and phosphorus metabolism. Moreover, the local hyperemia probably facilitates the secretion.

Monatsschrift für Psychiatrie und Neurologie, Basel

100: 1-128 (Sept.) 1938. Partial Index

Pathogenesis and Clinical Aspects of Subarachnoid Hemorrhages (Hemorrhagic Leptomeningitis). I. Scheinker.—p. 9.
Amnesic Aphasia, Visual Aphasia and Disturbance in Optic Conception. H. Scheller.—p. 33.
*Polyneuritis After Oral Administration of Medicaments Containing Sulfanilamide. J. Rost.—p. 92.
Disturbances in Optic Perception in Hypoglycemia. A. Weil.—p. 98.

Polyneuritis Following Sulfanilamide. — Rost directs attention to undesirable secondary effects that develop following the administration of a sulfanilamide preparation that is widely used in the treatment of gonorrhea (uliron). Although the therapeutic results obtained with this preparation have on the whole been gratifying, disorders such as headaches, intestinal disturbances, vomiting and morbilliform and urticarial exanthems have been observed in about 30 per cent of the treated cases. These disorders are usually observed on the tenth day of the treatment but they disappear, after the medication is discontinued, without causing further sequels. Recently, however, polyneuritic symptoms have been observed. After citing a case that was described by Hüllstrung and Krause, Rost describes two cases of his own. Both patients developed a polyneuritis, with special involvement of the motor component, after they had been subjected to sulfanilamide therapy, under the influence of which the gonorrhea had promptly subsided. The course of the polyneuritis was slow in both cases, but by the administration of vitamin B_1 the improvement could be somewhat accelerated. In the discussion of the pathogenesis of the polyneuritis it is pointed out that gonorrheal disorders as such have been known to cause neuritic symptoms in rare cases. However, in the first one of the cases discussed there was evidence that the polyneuritis was caused by the medication and not by the gonorrhea. Attempts have been made to solve the problem by animal experiments, but these have produced no satisfactory results as yet. It appears probable that the dosage of the preparation plays a part. In all cases in which neuritic disturbances were observed, the total dose was far in excess of that recommended by Schreus. For this reason it may be hoped that in the future such complications may be avoided by careful watching of the dosage.

Schweizerische medizinische Wochenschrift, Basel

68: 1181-1200 (Oct. 22) 1938. Partial Index

Union and Division as Formative Processes in Embryologic Development. G. Wolf-Heidegger.—p. 1181.
Incidence of Pulmonary Syphilis in Portugal. F. Wohlwill.—p. 1186.
Bilirubin and Lipochromes in Blood. A. Gigon and M. Noverraz.—p. 1189.
*Acute Nicotine Poisoning During Extermination of Parasites by Means of Spray Method. H. Wehrlin.—p. 1191.

Acute Nicotine Poisoning from Parasiticide.—Wehrlin reports the clinical history of a man aged 24 who was hospitalized with tetaniform spasms in all four extremities, abdominal spasms, nausea, headache, excessive perspiration and tachycardia. The spasms disappeared after a short time. After describing the results of the general examination, the author says that the diagnosis proved difficult at first but that poisoning was thought of. The anamnesis revealed that the patient, who was a gardener, had sprayed a parasiticide consisting of a nicotine solution. The author cites similar cases from the literature which seem to indicate that the symptomatology of this type of nicotine poisoning varies considerably. Moreover, the symptoms resemble those of other intoxications and consequently do not permit a diagnosis. The latter is made possible by an exact anamnesis and by the chemical or biologic demonstration of nicotine in the excreta. The biologic test is based on the fact that, if a nicotine solution is dropped on the tongue of a frog, the animal responds by a peculiar curving contraction of the leg onto the back. In fatal cases, all organs contain nicotine. Since parasiticides that contain nicotine are used widely in agriculture and horticulture the author advises that, if acute intoxications are observed in gardeners and persons with similar occupations, nicotine poisoning should be promptly considered.

Atti d. Soc. Ital. Ostetricia e Ginecologia, Rome

84: 785-880 (Sept.-Oct.) 1938. Partial Index

Technic and Value of Mastography After Introduction of Opaque Liquids in Galactophoric Ducts. A. Gusso.—p. 804.
Gangrene of Feet from Ergotamine Injections in Early Puerperium. A. Gusso.—p. 826.
*Amount of Ascorbic Acid in Human Placenta. F. Rossi Marcelli.—p. 842.
Interstitial and Submucous Fibromas of Uterus with Amenorrhea and Positive Friedmann Reaction. A. Duca.—p. 869.

Ascorbic Acid in Human Placenta. — Rossi Marcelli made quantitative determinations of the amount of ascorbic acid contained in ninety normal human placentas at different periods of evolution of pregnancy and at full term. He found that it varies within 1.32 and 1.58 mg. of ascorbic acid for each gram of placenta during the first six months of pregnancy and within 1.45 and 1.8 mg. of the acid for each gram of placenta during the last three months, after which it rapidly increases so that at full term it is twice as much as it was previously (within 3.96 and 4.85 mg. of ascorbic acid for each gram of placenta).

Gazetta degli Ospedali e delle Cliniche, Milan

59: 1011-1032 (Oct. 9) 1938

*Transfusion of Preserved Blood. I. Mingazzini.—p. 1011.
Free Intra-Articular Bodies in Chondrosarcoma of Astragalotibial Joint. C. Leonardo.—p. 1017.

Transfusion of Preserved Blood.—Mingazzini gave preserved blood transfusions to twenty-six patients suffering from gastric or duodenal ulcers or from gastric cancer. The procedure was resorted to before or after a surgical intervention and in some cases transfusion was repeated. The blood had been stabilized by addition of sodium polyacetylenedioxisulfonate and preserved for from one to twelve days when it was administered to the patients. The results were similar to those which could have been obtained from transfusion with fresh pure blood. Unpleasant reactions, fever and changes in the urine did not take place. The crasis of the blood and the general condition of the patients improved in all cases. No doubt the administration of fresh pure blood is preferable whenever possible. But when not obtainable, as in many instances, blood stabilized with sodium polyacetylenedioxisulfonate and preserved for from one to twelve days can be used with safety. The technic for preparation of the blood and for transfusion is easy, the biologic and therapeutic properties of the blood do not diminish and the results are satisfactory.

Giornale di Clinica Medica, Parma

19: 1227-1334 (Oct. 10) 1938

Experimental Investigations on Relation Between Glycemia and Chloremia. G. Battistini and P. Cavazzini.—p. 1227.
Research for Presence of Iron in Human Testicles. I. Rizzi.—p. 1252.
*Metabolism of Creatine Bodies in Exudative Diatheses. C. Magi.—p. 1279.
Evaluation of Allergy in Tuberculosis in Adults by von Gröer's Allergometric Method. Irene Miller.—p. 1295.

Metabolism of Creatine Bodies in Exudative Diatheses. —Magi found, in twenty-three infants and children who had an exudative diathesis, that the elimination of creatine and creatine bodies through the urine is diminished, in relation to normal, whereas that of creatinine is increased. According to the author, the diminished elimination of creatine and creatine bodies in the presence of an exudative diathesis is due to defective development of the muscles from alterations of the cellular metabolism of proteins and nitrogen substances with a consequent imperfect assimilation of the substances by the muscular tissues. The metabolic disorders originate in congenital endocrine and neurosympathetic disturbances.

Minerva Medica, Turin

2: 389-412 (Oct. 20) 1938. Partial Index

Pyretotherapy and Index of Opsonins in Blood. G. Vernoni and A. Pirone-Nacconetschnii.—p. 389.
*Lymphogranulomatosis Urethritis (Nicolas-Favre) in Women. A. Midana and Rita Leone.—p. 398.

Lymphogranulomatous Urethritis in Women.—Midana and Leone report eight cases of lymphogranulomatous urethritis in women. The patients had presented inguinal adenopathy in the past for periods of from one to five months. They com-

plained of a burning sensation at the urethra and had lymphogranuloma at the anus, rectum, vulva or external genitals and a positive Frei test. The urethral lesions could be seen either by simple examination or by urethroscopy. They were ulcerous, vegetative, associated ulcerous and vegetative, inflammatory or sclerotic and, in some cases, they were continuous with the external esthiomene. The disease was secondary to vulvar, anal, rectal or genital involvement in all cases. In certain cases, however, chronic lymphogranulomatous urethritis develops as the primary focus. When the disease is secondary to a primary lymphogranulomatous lesion, it originates in a propagation of the virus through the lymphatic channels with consequent disturbances of the local lymphatic circulation and damage of the tissues from direct contact with the virus.

Anales de la Facultad de Medicina, Montevideo

22: 691-892 (Nos. 9-10) 1938. Partial Index

Infraperitoneal Drainage at Lumborenal Region. L. A. Surraco.—p. 691.
Acute Form of Chagas' Disease: Case. R.-V. Talice, A. Alambarri and U. Regules.—p. 761.
Intestinal Perforation in Amebiasis. D. Mosto.—p. 836.
*Rheumatism from Focal Infection. D. Quiroz.—p. 862.

Rheumatism from Focal Infection.—Quiroz made a clinical and roentgen study of fifty cases of rheumatism caused by focal infection from the teeth in thirty instances, the tonsils in seventeen and both the teeth and tonsils in three. Rheumatism from dental or tonsillar infection is either chronic, recurrent or polyarticular and it causes neither cardiac nor renal complications. Two of the fifty cases reported by the author were complicated by nonsuppurative, painful mastitis. He calls attention to the fact that mastitis has not been previously reported as a complication of focal infection. Treatment of the condition is surgical. It consists in early removal of the infectious focus followed by the proper medical, symptomatic, physicotherapeutic, antiallergic endocrine, dietetic and hygienic treatment.

Archiv für Kinderheilkunde, Stuttgart

115: 65-128 (Oct. 14) 1938

Periostal Bone Changes in Young Nurslings. O. von Chiari.—p. 66.
Diphtheria Infection and Antitoxin Content of Blood. K. Fejes.—p. 86.
Scarlet Fever and Eosinophilia. G. Tamási.—p. 90.
*Simultaneous Occurrence of Bronchial Asthma and Eczema and Their Reciprocal Modification During Childhood. F.-J. Casper.—p. 95.
Mastoiditis Complicated by Purpura Annularis Telangiectatica During Childhood. Margarete Wolf.—p. 114.

Simultaneous Bronchial Asthma and Eczema.—Casper says that all investigators agree that asthma and eczema are related and that they are symptoms of the same constitutional anomaly. The author investigated this relationship between asthma and eczema in 210 cases, giving especial attention to those in which asthma and eczema concur or alternate or in which eczema is to be found in the previous history. He describes in detail the histories of two children in both of whom there existed a hypersensitivity to milk, protein and in one case also to fats. Asthma developed for the first time when the eczema had disappeared and then the two disorders recurred alternately. In the second case there was evidence of a hereditary neuropathic component and the author suggests that neuropathy and exudative diathesis are related. He says that an allergic factor was noticeable in both cases but thinks that allergy does not explain the problem entirely. Studies on forty-two patients with chronic bronchitis and eczema revealed an asthmatic reaction in three. In all cases there were indications of a relation between eczema and bronchitis in that the bronchitic symptoms either alternated with the cutaneous manifestations or were accompanied by cutaneous exacerbations. The author further presents a report of seventy patients, thirty-nine of whom had both asthma and eczema and thirty-one only asthma. He shows that the essential factor in asthma as well as in eczema is the allergic constitution, which becomes manifest in a hypersensitivity of the organism to certain noxa, in vagotonic symptoms and in a tendency to eosinophilia. There exists a reciprocal action between eczema and asthma or bronchitis. If one of the two disorders is present in a severe form the other one is mild or is completely absent. In this connection the author tells of a man in whom attacks of asthma and eczema alternated and who, by preventing the healing of the eczema, was able to suppress the attacks of asthma. The author thinks that, in view of the evidence of connections between asthma and eczema, the two should be considered as one and he applies the term prurigo-asthma. He also suggests that, since asthma with the attacks of suffocation is usually dreaded more than the eczema with its itching, it might perhaps be advisable in cases of alternate appearance of the two disorders to prevent the complete healing of the eczema.

Beiträge zur klinischen Chirurgie, Berlin

168: 337-512 (Oct. 12) 1938. Partial Index

*Relationship of Bone and Joint Tuberculosis to Pulmonary Tuberculosis. H. Frank.—p. 337.
Injury to Biliary and Pancreatic Ducts in Course of Resection of Duodenal Ulcer. M. Paraskevas.—p. 350.
Chloride Elimination in Bile in Hypochloremic Uremia Following Operations on Bile Passages. W. Nell.—p. 359.
Ointment-Plaster Cast Treatment of Wounds. H. G. Burgass.—p. 383.
Traumatic Consequences to Extremities. H. Angerer.—p. 391.
Question of Congenital Origin of Lateral Fistulas and Cysts of the Neck. J. Marx.—p. 435.
Transurethral Resection in Carcinoma of Prostate. H. Wille-Baumkauff.—p. 467.

Tuberculosis of Bone and Joint and Pulmonary Tuberculosis.—Frank investigated the relationship between bone and joint tuberculosis and pulmonary tuberculosis in 1,003 patients treated at the sanatorium of Heuberg. He finds that the simultaneous existence of pulmonary tuberculosis and bone and joint tuberculosis in infants and children is frequent. This is explained on the basis of the frequency and the regularity with which infection and reinfection take place at that age, as well as on the feeble resistance of young bodies. Simultaneous pulmonary involvement is equally frequent in somewhat older children; most of these exhibit advancing ulcerative pulmonary tuberculosis. Simultaneous involvement of the pulmonary tissue between the ages of 10 and 30 years is rare. The fact that most of the cases of bone and joint tuberculosis occur at this age suggests the possibility of the existence of isolated chronic tuberculosis of a single system. A spreading ulcerative pulmonary tuberculosis occurred in 2.4 per cent of all cases of joint-bone tuberculosis. The rest of the cases of pulmonary involvement presented benign forms of the disease, which is explainable by the existence of positive allergy of the body in bone and joint tuberculosis. The author does not consider the coexistence of pulmonary tuberculosis a contraindication to operative treatment of bone foci. Frequently the removal of a tuberculous focus exerts a beneficent effect on the entire organism.

Münchener medizinische Wochenschrift, Munich

85: 1537-1576 (Oct. 7) 1938. Partial Index

Puerperal Sepsis. W. Schultz.—p. 1537.
Whooping Cough in Adults. H. Schlack.—p. 1541.
*Benign Gastric Ulcers in Pernicious Anemia. W. Haring.—p. 1544.
*Critical Remarks on and Own Experiences with Cyclocope of Samuels. R. Imbach.—p. 1545.
Experimental Gangrene by Heat Stasis and Anesthesia. H. Schwan.—p. 1546.
Duck Eggs as Cause of Two Epidemics of Enteritis in Military Kitchens. F. König.—p. 1550.

Benign Gastric Ulcers in Pernicious Anemia.—Haring points out that the close connections between the gastric mucosa and the hemopoiesis in the bone marrow lend considerable significance to the adenomas of the mucosa. In pernicious anemia there supposedly exists a disturbance in the so-called intrinsic factor which the healthy gastric mucosa probably forms by an incretory mechanism from the vitamin B_1 complex. Roentgenologic studies on the benign tumors which occur during pernicious anemia revealed to the author considerable secretory activity, and histologic studies on the tumors disclosed adenomas that were filled with colloid. He thinks that histologically they resemble the adenomas of the thyroid which occur in exophthalmic goiter or myxedema and suggests that the adenomas of the gastric mucosa might be related to the incretory activity. Surprising is the content in Hanse-

mann's bodies, the nature and the significance of which are still unknown. The author realizes that further investigations on true polyps of the mucosa in pernicious anemia will be necessary to clarify the relation between the two disorders and he hopes that this report will stimulate such studies. He suggests that all patients with pernicious anemia and those with funicular myelitis traceable to pernicious anemia be subjected to roentgenologic examination of the stomach to detect possible polyps of the mucosa. Moreover, if polyps are detected by surgeons or roentgenologists the patient under observation should be subjected to internal examinations in order to detect possible relations to pernicious anemia or other hyperchromic anemias.

Experiences with Cycloscope of Samuels.—The original and new opinions expressed by Samuels on the menstrual cycle, ovulation, the periodic fertility and the early diagnosis of pregnancy (see abstracts in THE JOURNAL, February 26, page 696, and April 9, page 1241) induced Imbach of the women's clinic in Zurich to investigate Samuels' claims. Imbach made his studies with the cycloscope recommended by Samuels. In a considerable number of women between 21 and 45 years of age and in one man, the reduction time was determined daily over a period of seventy-five days. As recommended by Samuels, curves were plotted of the reduction time in order to obtain so-called cyclograms. It was found that the technic is not as simple as had been suggested by Samuels and that there are many sources of error; for instance, it was found that the reduction time differs after the hands have been bathed in warm or cold water. Moreover, there is a difference whether a thick or a thin fold of skin is clamped off. The results obtained by the author do not tally with those obtained by Samuels. In not a single one of the normal persons subjected to the cycloscope test did he obtain curves that approximated those of Samuels. He reaches the conclusion that Samuels' spectroscope method does not reveal typical increases and decreases in the reduction time of the oxyhemoglobin within the monthly cycle and that the far-reaching and revolutionizing conclusions arrived at by Samuels lack a foundation that stands up under investigations.

Zeitschrift f. d. ges. experimentelle Medizin, Berlin

104: 249-464 (Oct. 12) 1938. Partial Index

Influence of Various Hormones on Prostate of Rat: Incretory Etiology of Hypertrophy of Human Prostate. F. Bühler.—p. 249.
Mechanism of Takata Reaction: I. K. Dirr and M. Platiel.—p. 292.
Causes of Differences in Results of Determination of Serum Bilirubin According to Hijmans van den Bergh and Jendrassik and Cleghorn. K. Dirr and N. Seroslis.—p. 337.
Temperatures and Vascular Conditions of Skin After Administration of Histamine to Human Subjects. O. Schwarer and R. Bauer.—p. 352.
*Effect of Intrapleural Injections of Hypertonic Solutions of Sugar During Exudative Pleurisy and Empyema. Bauer.—p. 364.
Influence of Sex Hormones on Bleeding Time and Coagulation Time. F. Bühler and L. Bayer.—p. 376.
Experimental Investigations on Antagonism Between Vegus and Thyroxine, with Observations on Action of Thyroxine on Heart. C. David.—p. 397.

Hypertonic Sugar Solutions Intrapleurally in Pleurisy and Empyema.—Bauer says that the conservative treatment of exudative pleurisy and the surgical treatment of empyema do not always produce satisfactory results and that a survey over the various methods of irrigation and instillation which have been recommended to accelerate cure and to avoid the formation of indurations and callosities reveals that none of the therapeutic methods satisfy completely. The results which Lexer obtained with the application of sugar to slowly healing wounds induced the author to resort to the intrapleural injection of hypertonic solutions of sugar in six cases of exudative pleurisy. It was thought that, by increasing the osmotic pressure in the exudate, a profuse fluid secretion could be obtained from the pleural endothelium. This was to prevent the formation of indurations or perhaps dissolve existing ones. It seemed possible also that the juxtapleural parts of the lung could be favorably influenced by withdrawing water from them. It was assumed that, following this discharge of fluid, a better blood perfusion would result. However, no adequate action could be obtained in this manner, because the greatly impaired pleura likewise absorbs sugar rapidly, so that there is no prolonged osmotic action. To be sure, the author thinks that Spengler's method of treating spontaneous pneumothorax by means of hypertonic solution of dextrose is to be recommended, because the hypertonic sugar solution noticeably stimulates the resorptive action of the pleura. The observation that a mild osmotic stimulus accelerates the resorption of exudates suggests that, in the case of many of the substances that have been recommended for irrigation or instillation, not the particular composition but the stimulus on the pleura promoted the resorption.

Zeitschrift für klinische Medizin, Berlin

135: 1-122 (Oct. 10) 1938. Partial Index

*Action Mechanism of Insulin. W. Brühl.—p. 1.
Gastric Secretion and Sodium Chloride Tolerance. T. C. Afendulis.—p. 29.
Clinical Characteristics of Bowl-Shaped Gastric Carcinoma. B. Fuchs.—p. 42.
Physical Investigations on Circulation in Hypertension. H. Siedek and F. Riedl.—p. 88.
Pathogenesis of Erythroblastic Anemia with Steatorrhea. F. S. P. van Buchem.—p. 95.

Action Mechanism of Insulin.—Brühl says that it is now generally conceded that insulin increases the motility and the secretory action of the stomach and that the last named action has led to the use of insulin in gastric diagnosis. In experiments on a large material, Kalk and Meyer gained the impression that in the action of insulin on the stomach the liver is in some manner involved. For this reason Brühl decided to investigate the action of insulin on the stomach of patients with hepatic diseases. He found that in severe disorders of the liver the latent period, that is, the time which elapses between the injection of insulin and the onset of the increased gastric secretion, is prolonged. He thinks that changes in the course of the blood sugar fluctuations are of causal significance in this delay: there is a flattening of the blood sugar curve, and the hypoglycemic values are reached later than is normally the case. Since the increase in gastric secretion that is observed after the administration of insulin is a result of the vagal irritation produced by the hypoglycemia, a retardation of the one must result in a retardation of the other. On the basis of blood sugar curves determined after administration of insulin in healthy persons and in patients with hepatic disease, the action mechanism of insulin is discussed and it is shown that the liver has an important part in the blood sugar fluctuations. It appears that the insulin blood sugar curve can be utilized for the detection of functional disturbances of the liver. However, the determination of the latent period of the gastric effect of insulin by means of the fractionated withdrawal of the gastric contents has sufficient reliability as a diagnostic aid only in the presence of severe hepatic impairment.

Zeitschrift f. menschliche Vererbungslehre, Berlin

22: 129-260 (Sept. 20) 1938. Partial Index

Historical Remarks on Term and Definition of "Diathesis." M. von Pfaundler.—p. 129.
Familial Occurrence of Cleft Hand and Cleft Foot. Leonore Liebenam.—p. 136.
Endemic Goiter and Malformation. L. von Unterrichter.—p. 160.
*Heredity of Allergic Diseases, Especially of Hay Fever. H. Sachsse.—p. 165.
Investigations on Twins and Families Regarding Hereditary Pathology of Hyperthyroidism. W. Lehmann.—p. 182.
What Conditions in Microscopic Structure of Chromosomes Are Responsible for Recessivity of a Gene. Gertrand Hasse-Bessell.—p. 258.

Heredity of Allergic Diseases.—In this discussion of the heredity of allergic diseases, Sachsse gives particular attention to hay fever. He reports studies on the families of thirty-eight patients with hay fever. The reports of some authorities on allergic diseases induced him to inquire in his hay fever patients and their families for disorders such as conjunctivitis during the spring months, asthma after contact with certain odors and substances, gastrointestinal disturbances after the ingestion of certain foods, and disorders such as urticaria, Quincke's edema, eczema, cholelithiasis, nephrolithiasis, gout, sciatica, rheumatism, migraine, exophthalmic goiter and gastric ulcer. On the basis of his studies he answers the question regarding the hereditary transmission of an allergic predisposition in the affirmative. However, environmental factors seem

to play an important part in the elicitation of an allergic symptom, so that it is possible that in one generation the allergic disposition is not so evident and that in an otherwise evidently dominant transmission it can be found that one generation has been missed. The author gained the impression that for a "strong" allergic predisposition it is necessary that at least two genes be present which carry an allergic tendency. Hay fever seems to become manifest only if at least two such genes concur, that is if either a "strong" predisposition is transmitted from one parent or a "weak" monomeric one from both parents. The author thinks that if two or more factors play a part it is understandable why the family anamnesis is not always so clear as is the case of monomeric dominant transmission. In this connection the author cites observers who assume a recessive transmission. In his own material the recessive transmission was contraindicated also by the fact that there were practically no marriages in relationship in the hay fever families investigated by him. He points out further that Hanhart's observation that in case of allergy in both parents not three fourths but only two thirds of the children are allergic might indicate a dimerous dominant transmission. He concludes that a complete and exact explanation of the mode of hereditary transmission requires further serial statistical studies, and especially investigations on twins.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 4649-4776 (Sept. 24) 1938. Partial Index

*Therapy of Encephalitis and of Related Neurotropic Infections of Nervous System. W. M. van der Scheer and R. Zijlstra.—p. 4666.
Route of Inspiratory Air Current and Possibility of Aspiration from One Side of Nose into Lung of Same Side. H. A. E. van Dishoeck.—p. 4673.
Measurement of Blood Pressure and Pulse Frequency in White Person in the Tropics and in Colder Climates. W. Radsma, J. T. Meijman and G. G. A. Mastenbroek.—p. 4679.
Clinical Course of Fibrosarcoma, Spindle-Cell Sarcoma and Angiosarcoma of Soft Tissues. H. L. van Viersen Trip.—p. 4692.

Therapy of Encephalitis.—Van der Scheer and Zijlstra direct attention to the use of methenamine in the treatment of encephalitis and of related neurotropic infections. After reviewing the literature on this treatment, they report the results obtained with it in more than 200 cases at the clinic for psychiatry and neurology in Groningen. A tabular report indicates that the material included patients with various forms of encephalitis, disseminated and transverse myelitis, postencephalitic parkinsonism, chorea minor, herpes zoster, radiculitis, Landry's paralysis, polyneuritis, poliomyelitis and others. On the basis of their experiences the authors recommend this treatment. They administer the methenamine in the form of a 40 per cent solution by means of intravenous injections. The individual dose is 10 cc., which usually is given every other day. The total dose is from 100 to 200 cc.

Acta Radiologica, Stockholm

19: 207-312 (Sept. 30) 1938. Partial Index

*Roentgen Diagnosis of Tuberculous Spondylitis. N. Westermark and Gösta Forssman.—p. 207.
Transparent Gas-Containing Cleft Formations in Gallstones and Their Significance in Roentgen Diagnosis. Å. Åberlund.—p. 215.
Sigmoid Volvulus of 360 Degrees Without Strangulation and With Insignificant Symptoms. B. S. Holmgren.—p. 230.
Some Results of Irradiation with Soft Roentgen Rays at Small Focus Skin Distance (Contact Therapy). D. den Hoed.—p. 239.
Unusual Ossification Center in Pelvis. Gösta Lindberg.—p. 350.
Diagnosis of Extrapleural Abscess. H.-G. Skarby.—p. 259.

Roentgen Diagnosis of Tuberculous Spondylitis.—Westermark and Forssman demonstrate that from the roentgenologic point of view tuberculous spondylitis can be divided into a focal and a diffuse osteitis. The focal osteitis is more common in adults and the diffuse osteitis is more frequent in children. In focal spondylitis two different types are to be differentiated. One type is surrounded during the early stage by a circumscribed otosclerosis and by periosteal deposits; the other type is characterized by a rounded or irregular sequestrum and a rarefied border zone. Both types of focal spondylitis are localized most frequently in the anterior lateral border of the vertebral body. In focal spondylitis roentgenologic diagnosis is possible at an early stage, whereas in diffuse spondylitis the roentgenologic discovery is usually rather late.

Hospitalstidende, Copenhagen

81: 917-944 (Sept. 20) 1938

*Treatment of Gangrene. H. Christensen and S. Hansen.—p. 918.
Polycythemia Treated by Irradiation of Pyloric Glands and Brunner's Glands. F. Andersen, T. Geill and E. Samuelsen.—p. 933.
Experiences with Meltzer-Lyon's Test. J. Agerholm-Christensen.—p. 940.

Treatment of Gangrene.—Christensen and Hansen report forty-eight cases of senile or diabetic gangrene of the extremities in thirty-three men and fifteen women with an average age of 69, given conservative treatment, supplemented by modern methods of wound treatment and modern treatment of diabetes. Attention was directed to keeping the dry necroses dry and to making the moist necroses dry in order that the necrotic tissue may mummify and be sloughed off; the result was often assisted by the amputation of one or two toes. The average hospitalization was ninety-five days. There was only one death from diabetic coma. Thirty-three patients (69 per cent) were discharged as recovered, twenty-four after conservative treatment, including slight operative intervention, nine after amputation of the leg.

Norsk Magasin for Lægevidenskapen, Oslo

99: 1065-1176 (Oct.) 1938

Acute Appendicitis in Small Children Aged Up to 5. P. Bull.—p. 1065.
*Cases of Progressive Muscular Dystrophy in Roving Norwegian Family. K. Wagner.—p. 1087.
Case of Spontaneous Hyperventilation Tetany. K. Thomassen.—p. 1099.
Widmark's Micromethod Applied in Determination of Ethyl Ether in Blood. O. Dybing.—p. 1105.

Progressive Muscular Dystrophy in Family.—Wagner examined fourteen of the affected members of the roving family in question, spread over the western part of Norway. There was paralysis without rigidity; of the patients with advanced atrophy accompanied by suspended or weakened tendon reflexes only three or four were so disabled that they had to be quiet. Of the thirty-five marriages that he traced in the family twelve, or about 35 per cent, were intermarriages, which he explains as due to social isolation. He concludes that a partially dominant factor is present, the affected persons being heterozygote with reference to the factor. The fact that three women, although undoubted bearers, have escaped the disorder may be accidental but may also mean that women are less liable to it than men. While the probability is not strong, he says, that nervous disorders are correlated with the muscular dystrophy, he found deafmutism in two cases in this family, epilepsy in one, manic-depressive insanity in one, mental unbalance in two, "queerness" in one and schizophrenia in one. There was also a criminal trend.

Ugeskrift for Læger, Copenhagen

100: 1045-1068 (Sept. 15) 1938. Partial Index

Serum Treatment of Type III Pneumonia. H. C. Gram.—p. 1045.
*Ascorbic Acid in Pregnancy, During Birth, in Puerperium and in Child's First Days of Life. A. Elmby and P. Becker-Christensen.—p. 1047.
Foreign Bodies in Heart. F. Mehlsen.—p. 1051.
"Scandinavian Disease" (Agranuloeytosis After Amidopyrine Preparations). Johanne Christiansen.—p. 1054.

Ascorbic Acid in Pregnancy, Puerperium and Newborn.—Elmby and Becker-Christensen made 4,000 determinations of the ascorbic acid in the blood, urine and milk in 200 women through the last five months of pregnancy and during birth and the puerperium, and determined the ascorbic acid in the umbilical blood and blood from the ear of the newborn. There was agreement between the ingested ascorbic acid and the spontaneous ascorbic acid concentration in the blood and milk. The titer of the serum ascorbic acid fell during pregnancy, whether the diet was deficient or rich in vitamin C, but not to excessively low values in the women whose diet was rich in vitamin C. The titer of the ascorbic acid in the serum in the newborn child depends on the concentration of the serum ascorbic acid in the mother and falls during the first ten days of life. The ascorbic acid concentration in the milk depends on the titer of the ascorbic acid in the mother's serum. By the additional administration of 100 mg. of ascorbic acid daily in the first ten days of the puerperium the ascorbic acid in the mother's serum and milk can be raised from subnormal to normal value. The titer of ascorbic acid in the child's serum follows that of the milk and therefore depends on the mother's diet.